LIPID PROFILE CHANGES AND ITS CARDIOVASCULAR EFFECT IN MENOPAUSAL WOMEN TAKING HORMONAL REPLACEMENT THERAPY (H. R. T.)

THESIS

FOR

MASTER OF SURGERY
(OBSTETRICS & GYNAECOLOGY)

BUNDELKHAND UNIVERSITY
JHANSI (U. P.)

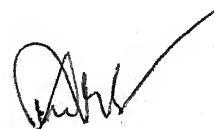1997   THINGBAIJAM PANTHOIBI

C E R T I F I C A T E

This is to certify that the work entitled "LIPID PROFILE CHANGES AND ITS CARDIOVASCULAR EFFECT IN MENOPAUSAL WOMEN TAKING HORMONE REPLACEMENT THERAPY" has been carried out by DR. THINGBAIJAM PANTHOIBI in the Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi.

She has put in the necessary stay in the department as per university regulations.
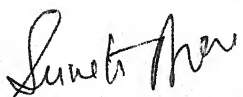
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were checked and verified by me from time to time.

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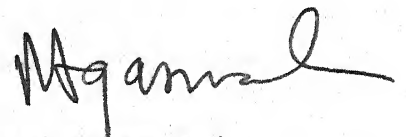
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Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi for her kind cooperation and constant encouragement during the period of this work.

I pay my thanks to all the teachers of the department of Obst. & Gynaecology, particularly Dr.(Mrs.) U. Agarwal, MS, Dr.(Mrs.) S. Kharkwal, MD, and Dr. B.D. Mathur, DHS, for their expert guidance throughout the course of study.

I deeply value the rich advice and assistance given by my colleagues to accomplish this study. My thanks are also due to my friends who have constantly encouraged and helped me in each and every step to complete this project.

I pay my regards and thanks to my parents for their sacrifice and moral support.

I pay my thanks to Shri Phool Chandra Sachan for his painstaking labour in typing of this project and Shri A.K. Tewari for laboratory assistance.

Lastly I bow in reverence to my lady subjects who have formed the material for present study. Nothing can replace them.

Dated : 28.10.96.

(Thingbaijam Panthoibi)

C O N T E N T

I N T R O D U C T I O N

INTRODUCTION

Menopause is the counterpart of menarche and refers only to cessation of menstruation. The climatric is the counterpart of puberty and is a transitional phase lasting 1-5 years during which genital organs involutes in response to the cessation of gonadal activity. Amenorrhoea after a simple hysterectomy does not lead to menopause as the ovaries will be still functioning. It is only when ovaries are removed with or without hysterectomy that one could call it a surgical menopause. The age at which menopause is reached varies with geographical, racial and nutritional factors. It does not depend on the age of menarche, marital status, parity, use of hormonal contraceptive, smoking or occupation. The age at menopause is around 49-50 years in most developed countries. In India, it varies from 44 to 50 years. In some women it sets in prematurely even before 40 years or it may be delayed to 53 years.

Around menopause due to primary ovarian failure certain important changes occur in the individual. These are :

1. Endocrinologic changes.
2. Metabolic changes.
3. Morphologic changes.

The oestradiol levels in the blood may be low in the menopausal women as compared to younger women. FSH is elevated 10-20 times the level seen during the follicular

phase of younger women. LH level is increased 3 times higher.

After menopause thyroid secretion is reduced. There is a decline in the adrenal androgen secretion with normal adrenal corticosteroid secretion contributing to protein catabolism. Bone, muscle and skin suffers most from this process of catabolism and over the years leads to flabbiness of muscles, thinning and wrinkling of skin and varying degree of osteoporosis. The decline in the oestrogen after menopause also lead to increase of blood cholesterol and phospholipid.

The changes are gradual and takes several years to become clinically appreciable. The skin which is the major target for oestrogen action because of oestrogen receptor slowly loses the subcutaneous fat and gets wrinkled and thrown into folds. The hair turn grey and there is mild hirsuitism due to relative androgen domi-nence. The breast tissue gets reduced and it becomes pendulous. Pubic hair gets reduced and there is decrease in fat in labia majora. The vaginal orifice becomes narrow and the mucosa becomes thinner and dry. Vaginal pH rises from 4.5 to 7 or 7.2. Bacterial infection occur easily. The uterus and cervix easily show gradual shrin-kage due to myometrial atrophy. The pelvic cellular tissue support becomes low resulting in varying degree of bladder and genital prolapse. Urethral mucosa becomes

atrophies.   There is increased risk of urinary tract
infection.

Menopause is associated with many after effects.
These can be broadly classified into :

Vasomotor symptoms   : Hot flushes,sweating.

Psychological symptoms : Depression, irritability,

fatigue and insomnia.

Sexual symptoms   :

Urinary symptoms   :

Perineopausal symptoms :

Vasomotor symptoms :   The hot flushes are due to
sharp rise in skin temperature, caused by peripheral vaso-
dilation and is accompanied by a transient rise in pulse
rate, profuse sweating, especially at night, irritability
and headahce.   The flushing last for 2-3 min at a time.
The vasomotor symptoms are hormone relayed.   It is generally
believed that women with surgically induced menopause have
a higher prevalence of hot flushes with increased severity
than women who experienced natural menopause, particularly
in the 1st year after ovariectomy.   Causation of hot
flushes is that hypothalamic thermoregulatory centre is
destabilized by oestrogen withdrawal.

Psychological symptoms are palpitation, nausea,
dizziness, headache, diaphoresis, insomnia and night sweats,
depression.   Sexual symptoms may be mostly attributable to
dyspnoea caused by dryness and deficient vascularity of the
vagina.   With oestrogen deficiency there is an increased

risk of introital colonization of enterobacteria leading
to urinary infection. Prolapse of bladder or urethra
may also contribute to urinary symptoms.

Apart from above symptoms following are
disorders resulting from or accelerated by menopause.

     a. Osteoporosis.

     b. Atherosclerotic cardiovascular change.

The rate of bone loss varies with age, sex and
site. By the age of 60 years, 10 times more forearm
fractures are seen in women than men. Oestrogens have
a protective effects on the bone as they influence calcium
absorption from the gut and reduce bone loss. With the
fall in oestrogen levels after menopause the bone is more
sensitive to the reabsorping action of parathyroid hormone
and vitamin D_3. With menopause therefore there is increased
absorption of calcium resulting in osteoporosis and
increased risk of fracture of the distal radius, vertebrae,
and proximal femur. The rate of bone loss is about 2% per
annum but that of spinal is 5%. There being greater loss
of trabecular than cortical bone. Oestrogen supplements
are more useful in the prophylaxis of osteoporosis in
menopause induced by oophorectomy and in these cases the
oestrogen therapy is started within 2 years of surgery.

There are several risk factors for osteoporosis.
These include low peak bone loss or positive family history
of osteoporosis, early menopause or oophorectomy alcohol,
cigarette consumption, multiparity and a sedentary life style.

In atherosclerotic cardiovascular changes there
is an increase in serum cholesterol and triglycerides.

It has been estimated that relative risk of
myocardial infarction among women who underwent bilateral
oophorectomy before the age of 35 years to be seven times
that of premenopausal women. While the increased risk is
readily evident in the group of women who suffered
premature menopause. The evidence in women who achieved
natural menopause is not so clear.

Hormone replacement therapy may be defined as an
attempt in the post menopause, to mimic by therapeutic
means the sex steroid status of an individual in her pre-
menopausal years. Thus the ideal regimen would seen to
be one which stimulates the physiology of the ovary itself
and in which natural human oestrogen with or without a
progesterone is delivered into the systemic circulation
achieving a concentration within the range found during
the menstrual cycle. Hormone replacement therapy (HRT)
should be achieved these end points safely with no trade
off in terms of breast or uterine oncogenesis, carbohydrate
intolerance or deranged coagulation and should promote a
lipid profile which will be reflected in clinical protec-
tive against coronary vascular and cerebrovascular disease.

Finally the ideal regimen should be inexpensive
and personally acceptable to the patient promoting a
feeling of well being in the present and of confidence
in the future.

With HRT there is reduction in bone calcium entering the circulation which was reflected in the fasting urinary calcium/creatinine ratio which also fell significantly as did the urinary hydroxyprotein/creatinine ratio. Plasma 1, 25 D rose but was matched by a rise in vitamin D binding protein and the free fraction of 1, 25D remain unchanged.

If HRT is begun in the early post menopausal years, it is possible that an increase in the bone mineral content(BMC) may occur. This may be due to refilling of the remodelling space opened up by the rapid phase of bone resorption in the immediate postmenopause or post oophorectomy. The duration of protective of bone mineral content appears to be for as long as ostrogen is administered. Menopause induced bone loss is greatest in the fiest 5-10 years after menopause and hence oestrogen replacement should be started as soon after menopause as possible to achieve the maximum benefit.

Oestrogen relieves hot flushes, particularly those occurring at night and the quality of sleep is often improved with a reduction in sleep latency and an increase in rapid eye movement episodes. The treatment response to either oral oestrogens or parenteral oestradiol takes 3-4 weeks for its beneficial effect in relieving vasomotor symptoms.

Post menopausal women receiving oestrogen replacement reported a positive effect on libido sexual activity,

It is popularly hypothesized that oestrogen cardioprotective benefit primarily by influecing the lipoprotein metabolism to achieve a favourable balance. In addition, oestrogen appear to have a direct effect on the vascular tree. Both oestrogen and progesterone receptors have been identified in the muscle wall of arteries.

Post menopausal oestrogen lower the serum concentration of HDL cholesterol particularly the HDL_2 subfraction in both cross sectional studies and clinical trials. Apo-lipoprotein A-1 which has an increased relationship to the risk of coronary heart disease is also raised among patients who receive exogenous oestrogens(Miller et al. 1991). Hormone replacement therapy thus favourably alters the LDL/HDL ratio in both the numerater and the demominater to reduce the cardiovascular risk.

Relatively high doses of oestradiol administered non-orally by intramuscular injection, subcutaneous implantation or as a percutaneous cream significantly reduce total and LDL cholesterol and elevation of HDL. Transdermal oestradiol patches delivering 50 ug or 100 ug/day reduce total and LDL cholesterol and increased HDL cholesterol. Oral and non oral therapies have quite different effects on plasma triglycerides. Oral therapies elevate the plasma triglycerides level whereas non-oral therapies do not.

Thus, all routes of oestrogen administration are appropriate for patient with familial hypercholesterolemic

and non oral oestrogens to patients with familial hyper-triglyceridemia.

Multiple alternative mechanisms for the protective action of oestradiol has been proposed :

1. Estrogens may prevent the oxidation of LDL which reduce its atherogenicity.

2. Estrogens may alter prostaglandin mechanism increasing prostacyclin levels and decreasing thromboxane levels both of these actions would prevent vasodilatation.

3. Estrogens may act directly on vessel walls to induce vasodilatation which is biologically possible since oestrogen receptors have been located at multiple site throughout the vascular system.

Types of hormone replacement therapy are oestrogen, combination of oestrogens and progesterone. Oestrogen can be synthetic and natural. Synthetic oestrogens are not preferred because these are structurally dissimilar to the oestrogen produced by the ovary. The synthetic oestrogen has much enhanced hepatic patency and can alter within liver the production rates of various factors involved in fibrinolysis and coagulation. Then significant changes are counted into clinical disease especially in older women. Oestrogen can be given orally percutaneously, subdermal implants, vaginal oestrogen, creams and pessaries and others - sublingual and injectables.

The minimum effective daily doses of various

orally administered progestogens when added for 10-12
days each calender month to oral and transdermal
oestrogens are :

Norethisterone	0.7/1.05-2.5 mg
L-Noregestrel	150 ug.
Dydrogesterone	10-20 mg
Medroxyprogesterone acetate: 10 mg.	

HRT COMBINATION PACKS

Oestrogen duration	Progestogen duration	Proprietary name
Conjugated egwine oestrogen 0.625mg/28 days	Norgestrel 150 ug/12 days	Prempak-C 0.625
Conjugated egwine oestrogen 1.25 mg/28 days	Norgestrel 120 ug - 12 days	Prempak-1.25
Oestradiol+oestrial (various doses)/ 28 days	Norethisterone 1 mg/10 days	Trisequens
Oestradiol valerate 2 mg/21 days	Noregestrel 500 ug/10 days	Cyclo-progynova 2 mg
Oestradiol valerate 1 mg/21 days	Noregestrel 500 ug/10 days	Cycloprogynova 1 mg

COMPLICATIONS OF HRT

Leg cramps, breast tenderness, limb pains, fluid
retention, eye irritation, nausea, and vaginal discharge,
occur in 8-21% of women taking HRT. Dyspepsia or gastro-
intestinal symptoms appear to occur in 3-4% of women
taking oral oestrogens. These can be abolished or minimized
by taking the tablet with food and or at bed time rather

than in the morning. If these strategies are unsuccessful then a non-oral route should be considered. Transdermal patch may cause skin reactions. Systemic absorption of intravaginal administration due to excessive use of oestrogen creams in the patient and her partner has been observed.

The implant site of subcutaneous implant may become infected and the implant may get extruded.

It has been demonstrated that no significant weight increase occur following therapy with conjugated estrogens or estradiol valerate neither has any weight increase been seen during estradiol medication) Launitzen, 1973).

Physical and psychological side effects associated with administration of progestogens.

Physical effects	Psychological effects
Abdominal cramps	Aggression
Accident prone	Anxiety
Acne	Apathy
Backache	Confusion
Breast tenderness	Depressed mood
Clumpsiness	Difficulty making decision
Dizziness	Emotionally labile
Flatulence	Foregetfulness
Fluid retention	Irrational
Generalized aches and pains	Irritability
Greasy skin	Pain attacks
Hot flushes	Poor concentration
Headache	Restlessness
Poor sleep	Tearfulness
Tiredness	
Weight gain.	

It has been observed that women who have experienced problematic premenstrual syndrome during the reproductive era appear more likely to suffer problem with progestogens when added to oestrogens post menopausally. The treatment of adverse effects of progestogens include:

- Reducing dose.

- Changing to another progestogens.

- Reducing the progestogen administration duration.

CONTRAINDICATION OF HRT

The safety concerns of HRT are either risks and contraindication. The risk is the likelihood of a condition developing as a direct result of treatment. With HRT this by and large, refers to the risk of cancer. A contraindication is a condition which is likely to be exacerbated or aggravated by taking HRT. Circumstances in which HRT should not be prescribed are termed absolute contraindication. Relative contraindications are situation in which HRT can usually be prescribed but careful assessment may be required before commencing treatment and only certain types of treatment or routes of administration may be advisable.

Absolute contraindications of HRT are :

- Endometrial cancer.

- Breast cancer.

- Known or suspected pregnancy.

- undiagnosed abnormal vaginal bleeding.

- Severe active liver disease with abnormal liver function tests.

Endometrial and breast cancer are responsive to oestrogens whether exogenous or endogenous. Pregnancy must be ruled out before starting HRT as spontaneous ovarian activity and ovulation may recur after many months of ovarian inactivity in perimenopausal women. The progestrogens could have a virilizing effect on the developing fetus if taken at a critical phase of organogenesis. A history of post menopausal bleeding demands appropriate investigation before commencing HRT. These patients require pelvic examination, cervical smear and dilatation and curattage or endometrial biopsy.

Epidemiological data on the incidence of thrombotic disease in oral HRT users are relatively sparse. It is unlikely that low doses of oestrogen used in oral HRT cause clinically relevant, fibrinolytic and coagulation changes. Any potential effect will be related not only to the dose of oestrogen but also perhaps to the route of administration with oral treatment or bolus of oestrogen passes to the liver via the portal vein after absorption of the steroid from gastrointestinal tract.

In the presence of severe active liver disease (with abnormal liver function tests) HRT should be withheld since a majority of oestrogen is degraded and metabolized within liver. If at all HRT has to be prescribed then - non-oral route would reduce the risk of compromising the liver further by avoiding the bolus of oestrogen achieved with oral therapy.

In patients with fibroid HRT may result in heavy withdrawal bleeding and others may achieve a considerable size. The risk of malignant change is less than 1%.

In women in whom all endometriotic tissue have been removed at surgery the chance of recurrence appear lower. In women previously diagnosed as having cystic hyperplasia it is believed that a follow up biopsy should be performed approximately 4-6 months after starting combined HRT to confirm that the endometrium has reversed to normal. The progestogen should be given at adequate daily doses and for an adequate duration each month per cycle at least for 12 days and perhaps even longer. Failure of an adequate progestational stimulus to reverse the hyperplasia should raise the question of hysterectomy. If atypical hyperplasia is diagnosed the hysterectomy is advisable before commencing the HRT.

HORMONAL REPLACEMENT THERAPY AND CANCERS

The use of oestrogen in HRT is associated with increased incidence of breast carcinoma and endometrial cancer. The use of unopposed oestrogen is associated with a higher risk of cystic adenomatous and atypical hyperplasia of the endometrium. Patients with atypical hyperplasia are more likely to have an associated endometrial carcinoma or develop it subsequently, the risk is as high as 45%. Important factors for development of endometrial cancer among oestrogen users are :

1. Duration of oestrogen use.

2. Dosage of oestrogen prescribed.

3. The use of progesterone in conjunction
   with oestrogen replacement.

Women who have used exogenous oestrogen for over
15 years found to have a relative risk of 20. The cellular
basis of the oestrogenic properties of progestogen on the
endometrium is fairly well established. Exogenous proges-
trogen reduce the total content of oestradiol receptors
in the endometrium. They also increase the activity of
the dehydrogenase that convert oestradiol to oestrone
which is a biologically less active oestrogen.

The duration of progestogens addition appear to
be of great importance. There is a significant reduction
in the incidence of hyperplasia from 20 to 30% with unopposed
cyclic oestrogens to 4% when progestogens were added for
seven days each month. With 10 days of progestogen a 2%
incidence of hyperplasia was reported with 12 days of
progestogens addition.

The role of oestrogen in causation of breast
cancer in women taking HRT is controversial. Several case
control studies using population controls studies indicates
that long term oestrogen use is associated with a small to
moderate increase in the risk of breast cancer. Using low
dose conjugated oestrogen does not appreciably increase
breast cancer risk. Oestrogen in combination with proges-
terone may actually increase the risk of breast cancer
over that associated with exposure to oestrogen alone.

Oestrogen use increases breast cancer risk in women with surgically proven benign breast disease. It has been noted that increased risk (1.8 fold) after 6 years of use with oestradiol while no such increase in risk was noted after use of conjugated oestrogen. The ovarian status influence both the risk of breast cancer as well as the rates of exposure to menopausal oestrogens.

It has been found that women who have had hysterectomy with ovaries retained to be at highest risk.

REVIEW OF LITERATURE

R E V I E W   O F   L I T E R A T U R E

The objective of hormone replacement therapy is obviously to enhance the potential benefits and minimize the risks. Over all, the outcome of therapy is reflected in lower mortality rates for those who have received treatment as compared with those who have not (Pititti et al, 1987; Hunt et al, 1987 and Henderson et al, 1991).

It is widely recognised that young women enjoy a significant degree of protection against ischemic heart disease when compared with men of similar age groups (Kannel et al, 1976). This sex difference diminishes with increasing age. This had led to the postulation that the hormonal mileau of the premenopausal woman plays an important cardio-protective role.

Rosenberg et al estimated the relative risk of myocardial infarction among women who underwent bilateral oophorectomy before the age of 55 years to be seven times that of premenopausal woman.

Gordon et al (1978) in the Framingham study showed that there was a significant excess incidence of coronary heart disease in women with surgical menopause.

Lauritzen et al (1973) has shown that the mechanism which occur in connection with hot flushes is better controlled by estrogen than by a placebo. After crossing over to placebo therapy from oestrogen treatment there is a worsening of this symptom.

Emotional function seem to be more favourably influenced than cognitive variables(Rausano et al,1975).

Anxiety and worry about oneself often disappear (Campbell and Whitehead, 1977).

Kantor et al (1968) and Michael et al (1970) in double blind studies on geriatric patients showed that estrogen therapy over more than 36 months improved learning ability and concentration. During placebo treatment of the same duration these parameters worsened.

Estrogen also improve the readings for the social contact and psychic alertness in aged women (Coldwell, 1952; Dueker, 1957; Evans and Marmorston, 1963; Coldwell and Watson, 1954 and Kopera, 1973).

Fedor-Freybergh (1977) demonstrated in a double blind trial that estrogen medication exerts positive influence on many psychological functions in the climacteric.

Improvement of memory was found by Campbell(1976).

Estriol increases attention and alertness. (Vanhulle and Deud, 1976). Insomnia and anxiety react more favourably to tranquilizer than to oestrogen, they react however, best to a combination of both(Shaffery et al,1969).

Cooper et al (1976) observed insomnia and arthralgia respond better to oestrogen than to placebo therapy.

Greenblatt et al (1950), Lauritzen (1973), Utian (1975) and Cooope (1976) have observed that hot flushes and profuse sweating are quickly and significantly reduced by estrogen treatment.

Coope et al (1976) observed that after a change from estrogen to placebo in cross over designed studied the hot flushes worsen considerably. After changing from placebo to estrogen the condition is considerably improved.

Estrogen medication also abolishes dizziness and tingling sensation and the concomitant rise of blood pressure which occurs with hot flushes (Lauritzen and Velibese, 1961).

Joswig-Priewe et al, (1973), Lauritzen and Muller et al (1977) observed that a consistent and favourable effect is also obtained by local and parental estrogen administration in atrophic condition, such as vaginitis and kraurosis vulva at vaginae when painful intercourse (dysparenic) is the problem.

Urethral carunde (Ectroprium urethrae) reacts very readily to estrogen, disappearing completely after a few weeks of estrogen treatment (Foffmann, 1950b; Lauritzen and Muller, 1977).

Smith et al (1977) observed that atrophic cystitis and urethritis with corresponding symptoms can certainly be ameliorated by estrogen medication as shown by urinary cytology and disappearance of the complaints.

Estriol, ethinyl estradiol cyclopentynol ether and estradiol valerate have been reported to improve first and even second degree shows incontinence (Lambillon, 1971; Wallner and Soost, 1971; Bol, 1950; Krong, 1959; Slundry, 1963; Daxelmueller et al, 1954).

Fedor-Freyberg (1977) observed that in some climacteric women libido is decreased because of nervousness, irritability and depressive mood, severe hot flushes and feeling of ill health. In such cases libido and sexual activity can be improved by estrogen treatment.

Master and Johnson et al (1977) observed that vulval or vaginal atrophy and inflammation lead to dyspareunia the treating of these symptoms with estrogens may also restore normal sexual feelings and activity by normalizing the structure and function of the organ.

Semmen and Wegner et al (1982) observed that oestrogen significantly increased blood flow to the vagina and the vulva.

Monly and Dallesy (1977) observed that estrogen improved vaginal lubrication.

These are prospective studies from Meemos et al (1975), Dequeker and Ferin (1977), Faruhjelhum (1976), Lindsay (1976), Nordin (1976), and Aitken (1974a and b) demonstrating that in non substituted castrated women the bone loss is significantly greater (as measured by the change in cortical thickness) than in patients with ethinyl estradiol or mesteranol in a daily dose of 20-25 ug.

Cristiansen et al (1981) observed that postmenopausal bone loss is primarily oestrogen dependent and may be prevented by oestrogen replacement therapy.

Nordin et al (1981) observed that major cause of postmenopausal osteoporosis appears to be an increase

in bone resorption.

Aitken et al (1971) observed that oestrogen effects on calcium metabolism are primarily mediated through an increase calcitonin activity.

Erikson et al (1988) obserbed that oestro- blasts were found to express oestrogen receptors.

Lindsay et al (1980) observed that the protective effect of oestrogens continue for as long as oestrogen is replaced. Stopping the oestrogen therapy results in acceleration of bone loss again. The rate of bone loss being identical to that of which occurs in the immediate postmenopausal layers. The net effect would be to buy time and delay the onset of clinical osteoporosis while oestrogen replacement is provided.

Prill and Lauritzen (1970) observed that estrogen therapy alleviates the periarticular complaints in post- menopausal patients in a high percentage of cases.

Lindsay et al (1984) observed that the minimum effective dose in one study was found to be 0.625 mg conjugated egwine, estrogen (Premarin) or its equivalent for oral therapy.

Ettinger et al (1987) observed that 1.5 gm of total calcium is combined with a reduced dose of conjugated oestrogen)0.3 mg) this offers the same protection as 0.625 mg conjugated oestrogens alone.

Christiansen (1990) observed that oestrogen is also effective when given by parenteral routes, provided

the serum oestradiol level is sufficient.

Gallaghen et al (1989) observed that addition of progesterone does not impair the bone preserving function of oestrogen. The minimum dose of oestrogen required to prevent bone loss was found by Horsman to be 15 ug of ethinyloestradiol per day. The equivalent dose of conjugated equine oestrogen being 0.625 mg.

The duration of protection of bone mineral content appears to be for as long as oestrogen is administered in sufficient dosage with bones loss occurring again after withdrawal and protection of bone mineral content over at least 10 years of HRT (Lindsay et al, 1980).

Rauramo and Punnonen (1976) have observed that atrophic changes which occur in the skin following oophorectomy can be prevented and reversed by the administration of estrogen.

The antiatrophic action of oestrogen is demonstrated by epidermal thickness measurements and by thymidine incorporation rate determinations. These findings have been confirmed to some extent by the radiological measurement of dermal thickness and by measuring the incorporation of thymidine and proline into human skin explats in the presence of estrone (Sharad and Marks, 1976; Marks and Shahrad, 1977).

Oestrogen treatment abolishes the temporary increase in blood pressure which accompanies hot flushes

(Lauritzen and Velibesi et al, 1961).

Notelovitz et al (1983) observed that oral
contraceptives containing synthetic oestrogen in relati-
vely higher doses are associated with an increased risk
of spontaneous thrombosis whereas natural oral oestrogen
replacement does not alter the clotting factors and has
no deleterious effect on coagulation.

Coope et al (1975) showed an increase in factors
VII and V and in increase in thrombin induced platelet
aggregation after 18 months of conjugated estrogen use.

Stangel et al (1977) reported that 14% of patients
in a control group and 57% of oestrogen treated women were
found to be hypercoagulable when multiple coagulation
factors were measured. A study conducted by Ross (1976)
indicated a protection effect of oestrogen in the post-
menopausal women with a risk of myocardial infarction of
0.43. This protection effect may not be maintained if a
patients smokes, 16 out of 17 postmenopausal women between
the age of 29 and 45 years who sustained nonfetal myocar-
dial infarction were found to be smoker and 9 out of these
17 women were receiving conjugated oestrogen. This study
suggested a 7.5 fold increase in nonfetal myocardial
infarction in the women of this age range who both smoke
and taking conjugated oestrogen.

Clinically an increase in thromboembolic events
has not been established in postmenopausal women on
oestrogen therapy in studies in which other risk factors

are controlled (Studd, 1978).

Utian et al (1977) observed that administration of 2-3 times the substitution doses (4 mg estradiol valerate or 5 mg conjugated estrogens) to 50 castrated women over a period of 1 year influenced diastolic pressure in only 2 patients.

Crane et al (1971) described five women who developed hypertension on low doses of conjugated oestrogen taken from 3-6 months in the menopause. All women subsequently become normotensive often discontinuation of estrogen therapy over a period of 1-7 months. Similar findings were described by Pleffer (1978) and Notelovitz (1979).

Notevolitz (1975) strolfeld (1977), Utian et al (1977) observed that no significant weight increase occurs following therapy with conjugated estrogens or estradiol valerate.

Aertgurts (1972) observed that there was improvement in wrinkles skin appearance elasticity and blood perfusion of skin after 6 and 12 months estriol succinate treatment (4 mg) in a high percentage of patients. Sanel (1982) observed that oestrogen has an effect on perception and skin sensitivity.

Boyd et al (1973) observed that administration of various estrogens, such as ethinyl estradiol, mestranol, conjugated estrogens, micronized estradiol, estradiol,

mestranol valerate and estrone sulphate nearly always produces a decrease of total lipids and of total cholesterol, especially of beta-lipoprotein cholesterol while increasing the phospholipid.

Ethinyl estradiol, mestranol and conjugated estrogen (in doses of more than 2.5 mg) usually elevate triglyceride levels (Furman, 1969; Lebech and Barggard 1973 and Boyd, 1973).

Estriol and Estradiol may sometimes even decrease triglyceride level if they are elevated (Proost et al, 1969; Larson-Cohn, 1976; Punnonen and Rauramo, 1976).

Hirvonen et al (1981) studied three groups of post menopausal women with estradiol valerate a dose of 2 mg/day and subsequently added 10 mg of norethindran acetate medroxy pregesteron acetate or norgestrel. Total cholesterol decrease in all groups by 10-18% from baseline values. Significantly, both estradiol norgestrel regimen decreased HDL by 20% during treatment. While no significant change in HDL was noted on medroxy progesterone therapy.

Tikaren et al (1978) reported an average 22% reduction in LDL concentration and 30% increase in HDL with administration of estradiol valerate.

Potocki (1971), Burch et al (1974) observed that frequency of coronary thrombosis has been seem to be significantly lower in women on long term estrogen treatment than in nontreated population of similar age and residence.

In the epidemiological study of Rosenberg et al
(1976), the relative risk of myocardial infarction in
long term estrogen treated patients was slightly lower
(relative risk 0.97) than in the control group.

Stampler et al (1985), Henderson et al (1991)
have obserbed a reduction in mortality from ischemic
heart disease and cerebrovascular accidents with post-
menopausal oestrogen replacement.

Connor et al (1989) and Miller et al (1991)
demonstrated that postmenopausal oestrogen administration
lower the serum concentration of LDL cholesterol and
increase the serum concentration of HDL cholesterol,
particularly the HDL_2 subfraction in both cross-sectional
studies and clinical trials.

Miller et al (1991) observed that apolipoprotein
A-1 which has an inverse relationship to the cardiovascular
morbidity.

Spellecy et al (1976) observed that aggravation
of glucose intolerance in women taking oral contraceptive
is primarily attributable to the progestin component and
not the oestrogen component of the oral contraceptives.

Spellecy et al (1987) demonstrated that natural
oestrogen replacement has no deleterious effect on the
carbohydrate metabolism of postmenopausal women.

Ballejo et al (1983) observed that use of
oestrogen actually improve glucose tolerance by enhance-
ment of insulin receptor binding.

Osteoporosis is the rare condition in the young
and healthy adults; however by the age of 75 years, fully
50% of U.K. resident females have sustained such a
reduction in their bone mineral content that they may be
labelled osteoporotic (Nordin, 1984).

Edwin Currie, the former U.K. Junior Health
Minister, stated that in 1935, 35000 women in England and
Wales sustained a femoral neck fracture, of whom 26000
(74%) were aged over 75 years. The age-specific incidence
of femoral beck fracture doubles every decade from age of
60 years (Gordan and Vaughan, 1977) , and the incidence
appears to be showing a true increase after allowance for
the present demographic increase of the population at risk
(Boyce and Vessey, 1985).

A marked rise in the bone turn over rate occurs
at the perimenopause (Heaney et al, 1978). In the human,
Eriksen et al (1987) have demonstrated the presence of
oestrogen receptors in cultured trabecular osteoblasts.
The rate of loss of trabecular bone in the immediate
post menopause may near 5% per year for natural menopause
and a nearly 9% per year after surgical castration
(Genant et al, 1983).

It has been shown that osteoblasts contain
progestogen receptors (Johnston et al, 1978) which also
bind glucocorticoids with high affinity. Progestogens may
also have a direct effect on the C cells of the thyroid

and promote skeletal protection via calcitonin release (Greenberg et al, 1986) as well as promoting bone formation (Lindsay et al, 1978).

US endocrinologist, Fuller Albright, first proposed that there was a link between ovarian failure and osteoporosis (Albright, 1940).

There is no over representation of highly parous women among patients who later develop osteoporosis and oral contraceptive usage may similarly provide a protective effect (Goldsmith and Johnston, 1975). Indeed calculation of aggregate sex steroid exposure in the period of fertility between puberty and menopause indicates that the longer an individual remains in the fertile 'window' , the less her risk of postmenopausal osteoporosis (Lindsay and Hart, 1984).

Christiansen et al (1987) found that a set of plasma and urinary biochemical parameters correlated well with current rates of bone loss measured over a 2 years period by single photon absorptiometry.

The Consensus Development Conference on Osteoporosis held at NIH, Bethesda in 1984, concluded that women should seek advice from a medical adviser in the immediate postmenopause as to whether hormone replacement therapy is or is not indicated.

The use of an added progestogen to induce endometrial shedding is generally seen as prophylactic against endometrial cancer provided that adequate duration

of dose is involved (Hunt et al, 1987).

In summary, they found that there was a relative risk of 1.59 (95%) confidence limits(1.18-2.10) of a breast malignancy in HRT users although interestingly less deaths from the disease were observed than would have been expected in the population studied, the relative risk of death being 0.55 (95% confidence limits 0.28-0.96).

Data from the United States have generally shown a protective effect from oestrogen against death due to ischaemic heart disease (Stampfer et al, 1985; Henderson et al, 1986), while in U.K., Hunt et al (1987) have shown a 0.7% relative risk of death from stroke among 'ever users' of HRT.

In the longer term it has been repeatedly shown that hormone replacement therapy by oestrogen alone (Lindsay et al, 1976; Horsman et al, 1977; Nachtigall et al, 1979) or in combination with a progestogen (Munk-Jensen et al, 1988) will halt postmenopausal or post oophorectomy losses of BMC (Bone mineral content).

The newer transdermal oestrogen patch has been shown to be effective in reducing the fasting urinary calcium creatinine ratio in all of its three available doses of 25, 50 and 100 ug. Chetkowski et al (1986) and prospective data on the ability of transdermal oestrogen to protect BMC in the medium term are urgently required.

Lindsay et al (1978) were the first to demonstrate that a progestogen might be capable of exerting a protective

effect on the skeleton. Norethisterone in a dose of 5 mg daily shows biochemical evidence of being protective to the skeleton (Selby et al, 1985) and Heany et al(1988) have shown prolonged suppression of bone specific alkaline phosphatase by morethisterone in the postmenopause indicating suppression of bone turnover.

Bone formation has been shown to be enhanced in the spayed beagle (Karambolova et al, 1986) by the use of continuous progestogen in the form of medroxyprogesterone acetate (MPA) , and there is good evidence that in the beagle model the drug shortened resorption times in the cortical bone remodelling unit (Snow and Anderson, 1985).

Ettinger et al (1985) found a 50% reduction in the occurrence of spinal and distal fractures in women who had been taking unopposed oestrogen compared with those never exposed to oestrogen.

Weiss et al (1980) showed that the risk of fracture of proximal femur or distal radius was reduced by 50-60% in women who had taken oestrogen as HRT at least 6 years.

Hutchinson et al (1979) found significant protection from oestrogen against femoral and radial fracture.

Using a prospective format, Riggs et al (1982) were able to demonstrate that in 144 patient-years of exposure to oestrogen and calcium, the vertebral fracture was 181 per 1000 patient-years and significantly less than

the rate of 834 per 1000 patient-years found in an untreated and age matched control group.

Exogenous unopposed oestrogen therapy was found to increase the risk of developing endometrial cancer 2.15 times as compared with risk in non users (Henderson 1989).

The increased risk is evident even after use of unopposed oestrogens for a period as short as 12 months and this risk persists long after the treatment is discontinued for as long as 10-15 years (Shapiro et al, 1985; Paganine-Hill et al, 1989).

Recent cohort studies (Paganine-Hill et al, 1989; Persson et al, 1989) supported the findings that increasing duration of oestrogen exposure is associated with increased risk of endometrial cancer but no minimum safe period has been found.

The benefit of adding a progestogen to oestrogen replacement therapy to reduce the risk of oestrogen induced endometrial cancer has been clearly demonstrated in clinical practice (Gambrell, 1988).

Exogenous progestogens reduce the total content of oestradiol receptors in the endometrium (Bayard et al, 1978; Martin et al, 1979). They also increase the activity of the dehydrogenases that convert oestradiol to oestrone which is a biologically less active oestrogen (Guspride, 1978; King et al, 1981).

The oestrogen-progestogens users were also noted to have significantly lower risks of endometrial cancer when compared to the untreated population (incidence 245.5 per 10,000) (Gambrell, 1988).

The duration of progestogen addition appears to be of great importance. There is a significant reduction in the incidence of hyperplasia from 20% to 30% with unopposed cyclic oestrogens, to 4% when progestogens were added for seven days each month (Whitehead et al, 1979).

Most case control studies fail to final evidence of significant overall excess risk in patients in ever users of ERT when compared to non users (Jick et al, 1980; Ross et al, 1980; McDonald et al, 19860 Brinton et al, 1986 and Wingo et al, 1987).

A meta-analysis of the literature on estrogen replacement therapy and breast cancer published since 1972 (Dupont and Page, 1991) suggested that the overall relative risk of breast cancer associated with HRT was low (1.07).

Several case control studies using population controls indicate that long term oestrogen use is associated with a small to moderate increase in the risk of breast cancer (Ross et al, 1980; Brinton et al, 1986).

Brinton et al reported overall relative risk of breast cancer (1.47) (95% CI : 0.9 to 2.3) after 20 years of use.

It is possible that duration risk relationship is affected by dosage and type of treatment and that the contradictory results could be due in part to these different aspects of therapy (Dupont and Page, 1991).

Hoover et al (1976) in a prospective study of 1,891 patients taking conjugated oestrogens noted increasing relative risk with follow up duration and progressed to 2.0 (96% confidence interval 1.1 to 3.4) after 15 years of use.

The large prospective study by Bergkvist et al (1989a) found increasing relative risk with increasing duration of treatment reaching a relative risk of 1.7 after nine years of treatment (95% confidence interval 1.1 to 2.7).

Dupont and Page (1991) quoted a relative risk of 1.08 (95%) confidence interval(0.96 to 1.2) for women who took 0.625 mg or less of conjugated oestrogen per day. This is consistent with the evidence that low dose conjugated oestrogen therapy does not appreciably increase breast cancer risk.

Bergkvist et al (1989) noted that the use of oestradiol was associated with a 1.8 fold increase in risk after more than six years of use (5% confidence interval 0.7 to 4.6) while no such increase in risk was noted after use of conjugated oestrogens or other types of oestrogens, mainly oestriol.

Oestrogens in combination with progesterone may actually increase the risk of breast cancer over that associated with exposure to oestrogen alone (Key and Pike, 1988).

Jick et al (1980) and Hulka et al (1982) found the subgroup of women with natural menopause on HRT at highest risk, while Hoover et al (1981), Hitt et al (1984) and Wingo et al (1987) found this true in women who had undergone bilateral oophorectomy. Ross et al (1980) and Hunt et al (1987) found women who have had hysterectomies with the ovaries retained to be at highest risk.

The use of an added progestogen to induce endometrial shedding is generally seen as prophalactic against endometrial cancer provided that adequate duration of dose is involved (Hunt et al, 1987).

Hunt and her colleagues (1987) found that there was a relative risk of 1.59 (95% confidence limits 1.18 to 2.10) of a breast malignancy in HRT users although, interestingly, less deaths from the disease were observed than would have been expected in the population studied, the relative risk of death being 0.55 (95% confidence limits 0.28 to 0.96).

Sullivan et al assessed the degree of coronary artery occlusion rising arteriography. They excluded women with mild or moderate stenosis and included only those with more than 70% occlusion. The age adjusted relative risk was 0.44 and this was not greatly influenced by age. Some

protection was observed in high risk groups e.g. the protective effect of HRT was stronger in those with higher as compared with lower levels of cholesterol.

Gruchow et al included a substantial minority with previous myocardial infarction, approximately 32% among oestrogen users and approximately 40% among non users. An occlusion score was derived and women were classified as having a low, moderate or severe score. The relative risk for severe coronary occlusion for current oestrogen users was 0.37 and for moderate occlusion was 0.59.

The nurses health study (Stampfer et al, 1985) is the largest prospective, cohort study to investigate the relationships between arterial disease risk and HRT. In 1976, 121700 females registered nurses completed a questionnaire and were enrolled. A further questionnaire was completed in 1978 and 32317 postmenopausal women without prior coronary artery disease were followed for an average of 3 years. Current users of oestrogens has a relative risk of 0.3, among past users this was 0.7.

According to Ottosson et al (1985) medroxy progesterone acetate causes potentially undesirable lipid effects. In a 3-months prospective study of postmenopausal women taking oral oestradiol 2 mg/day the addition of medroxy progesterone acetate, 10 mg/day reduced HDL-cholesterol by approximately 8% and HDL_2 cholesterol by as much as 18%.

MATERIAL AND METHODS

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MATERIAL AND METHODS

Present study was carried out in the Department of Obstetrics and Gynaecology and Department of Medicine, M.L.B. Medical College, Hospital, Jhansi during a period of twelve months.

SELECTION OF CASES

The menopausal women selected from out patient department coming with symptoms pertaining to menopause and the women on whom menopause was induced surgically by bilateral sulpingoophorectomy due to various disease. Total number of 50 subjects were studied. All the selected subjects were completely investigated by taking detailed history and physical examination. Special attention was paid to their past and family history to exclude risk factors before prescribing the hormones. The patients were excluded as per the following criteria :

1. Patients with liver disease, ischaemic heart disease, hyperlipidemia, diabetes, renal disease, hypertension, acute or recurrent vascular thrombosis.
2. Patients who had already taken hormones prior to commencement of hormone therapy.
3. Patients suspected of having breast tumour.
4. Patients on drugs that are liable to interfere with lipid metabolism and therapy influencing lipoprotein levels in the blood.

All the patients selected were of average built. They were divided into two groups :

Group A

This group consisted of patients having natural menopause of 6-18 months with mean duration of 9 months.

Group B

This group consisted of surgically induced menopause with age range of 45-50 years with mean age of 48 years.

METHODS

All the selected patients were given oral or written information about the trial and consent was taken from all of them. They were examined in details as regards to their name, age, detailed history of present illness, past history, family history, dietary history and history of intake of any hormonal preparation prior to commencement of therapy. A detailed general and systemic examination with special reference to height, weight, blood pressure was done.

The patients of the study group were followed for 1 year as given below :

1. Initial 3 months without any drug.

2. 9 months with the drugs of hormonal replacement therapy.

3. 3 months after withdrawal of HRT.

During the study period patients were followed monthly. In every visit they were asked for the following :

Hot flushes	Nausea
Headache	Insomnia
Dyspepsia	Discharge P/V
Heavyness in the lower abdomen.	Palpitation
Night sweats	Dizziness
Intestinal distension	Constipation
Burning micturition	Dyspareunia
Backache	Diaphoresis

EXAMINATION

General condition	Weight
Pulse & B.P.(Two mean values were taken after a resting interval of 30 minutes).	Per speculum examination to see vaginitis.
	P/V examination
P/V discharge	Any genital prolapse.

C.V.S. Examination :

Following laboratory investigations were done on every 3 monthly intervals.

a. Echocardiography (E.C.G.)

b. Glucose tolerance test (GTT)

c. Serum total Cholesterol (STC)

d. Serum triglycerides (STG).

e. High density lipoprotein (HDL).

Method of collection of blood

5 ml of blood was withdrawn from anticubital vein of the female in recumbent posture with all aseptic precautions, without producing venous stasis after 12-14 hours of fasting and after 10 minutes of supine rest.

Thus blood sample was allowed to settle down for half an hour and centrifuged and serum was preserved with standard precautions. Blood samples were collected during the following periods.

1. Within 3 months of surgically induced menopause.

2. After taking HRT for 3 months in group A.

3. After stopping HRT for 3 months in group B.

4. In patients with natural menopause who came to out patient department for 1st time with distressing menopausal symptoms.

Estimation of Lipid Factors

Serum total cholesterol, serum triglycerides and high density lipoprotein were estimated by diagnostic kits and VLDL & LDL were calculated by the

standard formula with the help of values of STC, STG
and HDL cholesterol.

1. Serum Total Cholesterol : Serum total cholesterol
    was estimated by commercial kits supplied by Ethnor.
    The basic principle is that cholesterol reacts with
    list   solution of ferric percholate ethyle acetate
    and sulphonic acid and gives a lavender coloured
    complex which is measured colorimetrically.

2. Serum triglycerides (STG) : It was estimated by
    acetyl acetone method. Principle behind this is
    that triglycerides are determined by measuring
    glycerol after the liberation from fatty acids by
    saponification. Glycerol is oxidized by sodium
    metaperiodate to formaldehyde which is directly
    proportional to the amount of triglycerides.

3. High Density Lipoprotein Cholesterol (HDI-c) : HDL-c
    was estimated by utilizing commercial kits supplied
    by Ethnor. Basic principle is that the HDL-c
    fraction is separated by using a prepitating reagent.
    The precipitate contains chylomicrons, VLDL, and LDL
    which are removed by centrifugation. The supernatant
    contains HDL-c which is estimated by HDL-c colour
    reagent which gives purple coloured complex. This
    is measured colorimetrically at 560 nm. The

intensity of colour developed is proportional to the concentration of HDL-c in the specimen under test.

5. Very Low Density Lipoproteins (VLDL) : It was calculated by the following formula given by Friedwald et al (1972). This formula is valid upto STG values of less than 400 mg/dl.

$$VLDL \ (mg/dl) \ = \ STG/5.$$

5. Low Density Lipoprotein (LDL) : It was calculated by the following formula given by Fredrickson DA (1972) :

$$LDL \ (mg/dl) \ = \ STC - (STG/5 + HDL)$$
$$= \ STC - (VLDL + HDL)$$

6. Estimation of LDL : HDL ratio was done with the help of values of LDL and HDL.

Thus, the values obtained were statistically analysed by using 't' test.

VAGINAL CYTOLOGY

The lateral wall of the upper third of vagina was lightly scrapped . This part of vagina is most sensitive to hormonal influence. The semen is stained with Shoir Stain.

OESTROGENIC EFFECTS

Oestrogen produces a cytological picture where mature epithelial cells are large eosinophillic cells with pyknotic nuclei. The background is clear containing a few bacteria and leukocytes. The number of mature eosinophillic cells/100 cells counted is expressed as the Karyopyknotic index. The squamous epithelium of vagina is divided into 3 layers. superficial, middle and deep. Vaginal smear where the basal cell predominates are typical of low oestrogen content e.g. menopausal . The presence of parabasal cells in vaginal smear indicates a low but not absent oestrogenic influence as seen in the normal menopause or in the normal vagina after menopause.

Hormonal preparation used : Conjugated oestrogen 0.625 mg once daily come in name of premarin.

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O B S E R V A T I O N S

The results are contained in the form of various tables.

In the present study we studied :

1. Effect of hormonal replacement therapy (HRT) in women with surgically induced and/or natural menopause in relation to their -

    a. Symptoms and after effects of menopause.

    b. Serum lipoprotein profile.

    c. Cardiovascular functions.

2. Comparison of the effect of HRT in women with natural menopause and women with surgically induced menopause.

Patients who had achieved menopause naturally (Group A) and came to out patient department with symptoms pertaining to menopause, were subjected for first blood sampling. Premarin (0.625 mg) was given once daily and blood sample was taken every three monthly intervals.

First sample of blood from surgically induced menopause (Group B) was taken on the day of discharge from the hospital after the operation. HRT was started from three months after operation. Second sample was taken on 6 month.

In both the groups of subjects i.e. A and B, HRT was withdrawn after giving for 3 months. Third sample was taken after stopping HRT for 3 months.

The results are mentioned in the form of various tables.

TABLE I : Distribution of the cases according to their age.

Groups	No.of cases	Age range (years)	Mean±S.D. (years)
A	25	45 - 55	47±2.05
B	25	45 - 50	48±2.15

TABLE II : Distribution of cases having H.R.T.

Groups	No.of cases	Percentage	
A (Natural menopause)	25	50.00	Premarin (0.625 mg)
B (Surgically induced menopause)	25	50.00	Premarin (0.625 mg)

TABLE III : Effect of HRT on patients of group A
(natural menopause).

Symptoms	Period (months)		
	0-3 (%)	4-6 (%)	7-9 (%)
Hot flushes & night sweat	35	5	40
Backache	35	2	45
Itching	25	2	20
Burning micturition	20	5	10
Discharge P/V	20	8	20
Ghabrahat	20	5	15
Insomnia	5	3	5
Palpitation	2	1	1
Diaphoresis	4	1	3
Genital prolapse	2	< 1	< 1
Dizziness	1	< 1	< 1
Dyspareuria	1	< 1	< 1
Intestinal distension and constipation	1	< 1	< 1

It is obvious from the table III that HRT
reduces post menopausal symptoms dramatically viz. hot
flushes and backache from 35% to 5% and 35% to 2%
respectively. The symptoms recur after stopping of HRT.
The percentage of patients nearing to previous where the
patients were not taking any HRT.

TABLE IV : Effect of HRT in patients of group B
(Surgically induced menopause).

Symptoms	Period (months)		
	0-3 (%)	4-6 (%)	7-9 (%)
Hot flushes & night sweat	50	5	40
Ghabrahat	40	10	30
Insomnia	40	10	30
Diaphoresis	40	10	30
Discharge P/V	80	12	20
Backache	30	5	20
Itching	5	0	3
Burning micturition	2	1	5

SERUM LIPOPROTEINS LEVELS

Before starting of HRT : Group A

In patients of group A, the serum lipoproteins
levels were as follows :

- One patient showed a rise in STC (228 mg/dl) and
  LDL (165 mg/dl).

- Five patients had serum STC in the range of 168-179
  mg/dl with mean value of 173.4 mg/dl.

- Nine patients showed serum STC in the upper margin
  of normal values (200 mg/dl).

- Nine patients had serum triglyceride levels in the
  upper limit of normal values.

- Three patients showed STC level near to lower margin of normal values.

- Thirteen patients showed their STC levels in the range of 78-98 mg/dl.

- The level of HDL were from 34 to 46 mg/dl with mean values of 39.56 mg/dl

- One patient had increased level of LDL.

- Thirteen patients had moderate levels of LDL.

- Eleven patients had their LDL level in the normal range from 110.8 to 115.4 mg/dl.

- Eight patients had their LDL levels near to normal balues i.e. 130 mg/dl.

- All the patients had their VLDL and LDL/HDL ratio in the normal range.

Group B

In patients of group B, the serum lipoproteins levels were as follows :

- Seven patients showed STC levels near to 200 mg/dl in the range of 192 to 198 mg/dl.

- Low levels of STC was observed in 5 patients.

- Twenty two patients had STC in the range of 170 to 188 mg/dl.

- Values of STC in 25 patients were as follows :

Upto 85 mg/dl	9 patients
85 - 95 mg/dl	11 patients
7 95 mg/dl	5 patients

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- Four patients showed HDL levels near to lower margin of normal values (30 mg/dl).
- Six patients had LDL levels in the moderate range (7 130 mg/dl).
- Three patients showed LDL levels near to 100 mg/dl.
- Remaining 16 patients had LDL levels near to upper margin of normal range (130 mg/dl).
- All the patients showed normal values of VLDL and ratio of LDL/HDL cholesterol.

After taking HRT for three months
Group A
- Two patients showed border line levels of STC.
- Low levels of STC were observed in 5 patients.
- Remaining 18 patients showed STC levels near to normal values.
- Two patients had HDL values lower than previous values viz. before taking HRT. Mean difference being 2.5.
- One patient had same value of HDL before and after taking HRT.
- Remaining 22 patients had HDL levels higher than the values of before taking HRT.
- Twenty patients had values of LDL in the normal range or near normal (/130 mg/dl).
- One patient had decreased 4.2 mg/dl of LDL values than previous values.
- Four patients showed LDL levels near to normal limit of moderate range (130-156 mg/dl).

- All the patients had LDL/HDL ratio in normal range and majority of patients had higher values of VLDL than previous values.

Group B

- 7 patients showed STC levels more than previous values.
- One patient had the same value of STC before and after taking HRT.
- 17 patients showed STC values lower than the values before taking HRT.
- One patient showed a rise in STC value after taking HRT for 3 months.
- One patient had same value of STC before and after taking HRT.
- Remaining 23 patients showed the following pattern of STG levels :

0 - 5 mg/dl (mild)	16 patients
5 - 10 mg/dl (marked)	7 patients

- Rise in level of HDL was observed in 19 patients after taking HRT as follows :

Upto 2 mg/dl	6 patients
3 - 4 mg/dl	10 patients
7 5 mg/dl	3 patients

- Three patients showed same HDL levels even after taking HRT.
- A decrease in HDL levels was observed in 3 patients.

- One patient showed raised level of LDL. The difference being 1.8 mg/dl.

- Remaining 24 patients showed reduced levels of LDL after taking HRT.

- All the patients had ratio of LDL/HDL in normal range and higher VLDL than previous values.

After withdrawal of HRT for 3 months

Group A

- 15 patients showed STC values more than 200 mg/dl.

- Remaining 10 patients had STC Levels in the range of 180-200 mg/dl. Mean being 187.5 mg/dl.

- Three patients showed same values of STG after withdrawal of HRT as with HRT.

- Remaining 22 patients showed a rise in STG levels after withdrawal of HRT. The difference ranging from 12 to 10 mg/dl.

- Out of 22 patients 13 showed mild increase in STG levels (0-5 mg/dl) and 9 patients showed a rise of 5-10 mg/dl.

- Same levels of HDL were observed in 2 patients.

- 14 patients showed mild decrease (0-2 mg/dl) in HDL levels.

- Moderate decrease in HDL levels was observed in 5 patients after withdrawal of HRT.

- Six patients had marked decrease in HDL levels.

- Three patients showed higher values of LDL
  i.e. $>$ 160 mg/dl.

- Another three patients showed $<$ 130 mg/dl LDL levels.

- Rest of 19 patients showed LDL values near to lower
  limit of border line range via 130-150 mg/dl.

- All the patients had ratio of LDL/HDL in normal range.

Group B

- Two patients showed lower value of STC than the value
  after taking HRT.

- Remaining 23 patients showed a rise in STC value
  however, this rise was eratic. The difference
  being 2 to 12 mg/dl.

- Three patients had same values of STG while reamining
  22 patients showed a rise in STG levels as given below:

0 - 5 mg/dl	12 patients
$>$ 5 mg/dl	9 patients

  One patient showed a decrease in STG level than
  the value of after taking HRT.

- The value of HDL remained same in 1 patient. While
  in 23 patients the HDL levels fell down and in one
  patient there was a rise in HDL level of 1 mg/dl.

- Nine patients showed moderate level of LDL ($>$ 130 mg/dl).

- Two patients had low levels of LDL after stopping
  HRT for three months.

- Remaining 14 patients had LDL levels near to lower
  limit of moderate level of LDL (130 mg/dl).

- One patient showed reduced level of LDL after stopping HRT than after HRT values.
- Remaining 24 patients showed a rise in LDL levels after stopping HRT than the value after HRT.
- All the patients had ratio of LDL/HDL in normal range. There was a rise in VLDL levels than after taking HRT.

VAGINAL CYTOLOGY

Group A

Out of 25 patients, 4 had discharge of per vaginum. and subjected for vaginal cytology. Vaginal smear showed dominance of parabasal cells. This indicates low oesteo-genic effect before the commencement of HRT.

After taking HRT for 3 months, 2 patients had discharge per vaginum. The smear showed dominance of basal cells. After withdrawal of HRT for three months four patients had discharge of per vaginum and were subjected for vaginal cytology which showed presence of basal cells.

Group B

Before the commencement of HRT, 20 patients had discharge per vaginum. Out of which 18 patients showed dominance of superficial cells. Two patients showed dominance of basal cells in vaginal smear.

After taking HRT, 3 patients had discharge per vaginum. Their cytology examination showed dominance of basal cells.

Group A — HOT FLUSHES & NIGHT SWEAT
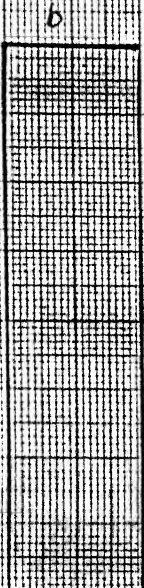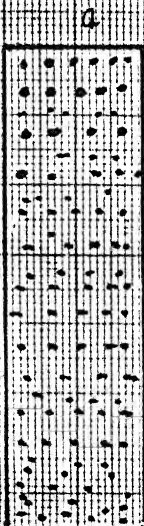
a — Before H.R.T
c — After H.R.T × 3 months
b — After withdrawal of H.R.T × 3 months
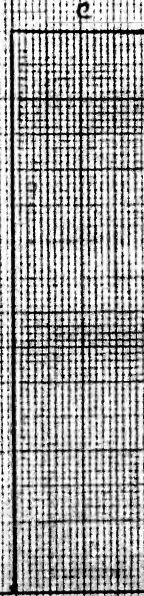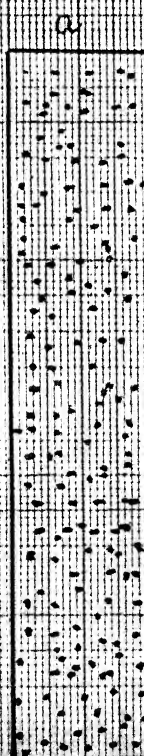
a — Before HRT
b — After HRT × 3 months
c — After withdrawal of HRT × 3 months

EFFECT OF HRT ON BACKACHE

GROUP-A

GROUP-B

(a) - BEFORE HRT

(b) AFTER HRT FOR 3 MONTHS

(c) AFTER WITHDRAWAL OF HRT FOR 3 MONTHS
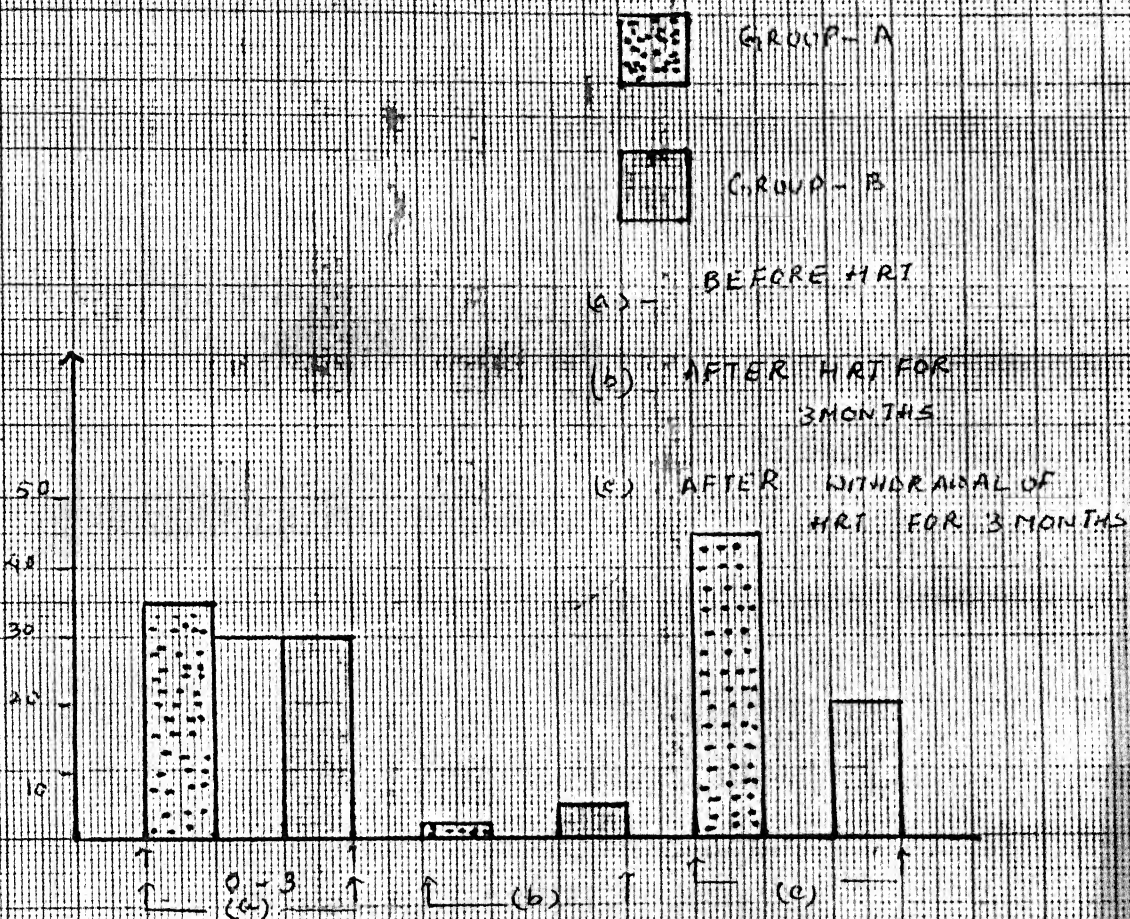
DISCHARGE PER VAGINUM

Group A

a — ▨ BEFORE HRT

b — ▨ AFTER HRT FOR 3 MONTHS

c — ▨ AFTER WITHDRAWAL OF HRT FOR 3 MONTHS

Group B

a — ▨ BEFORE HRT

b — ▨ AFTER HRT FOR 3 MONTHS

c — ▨ AFTER WITHDRAWAL OF HRT FOR 3 MONTHS
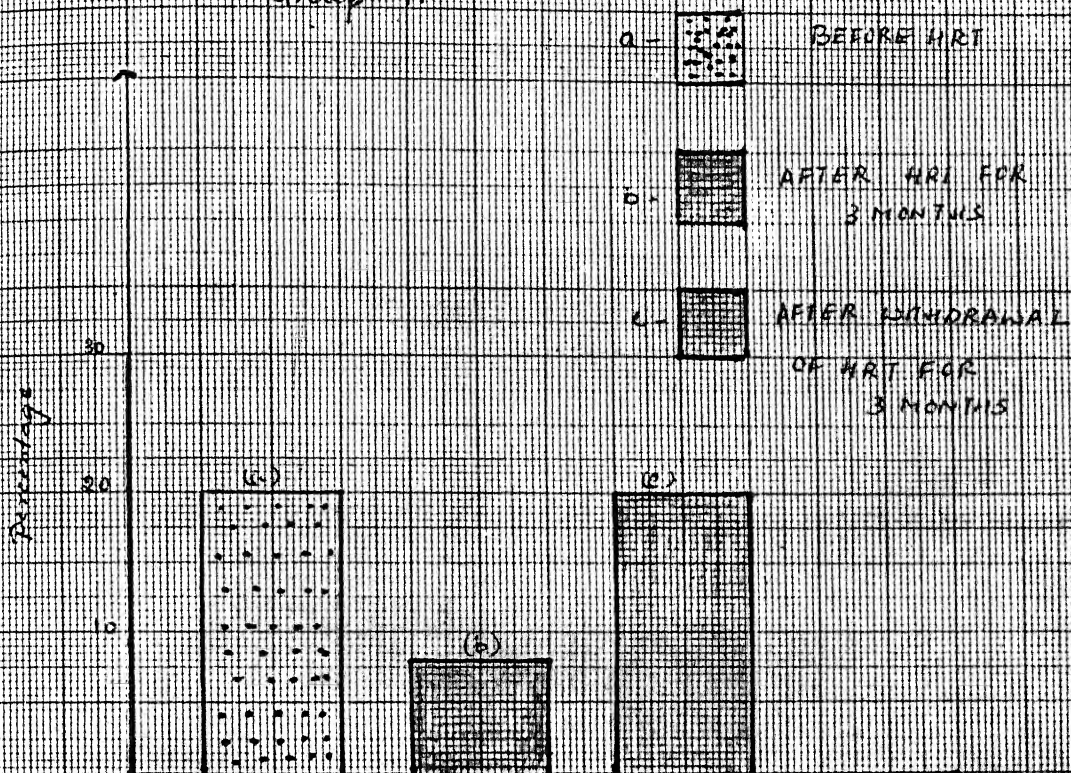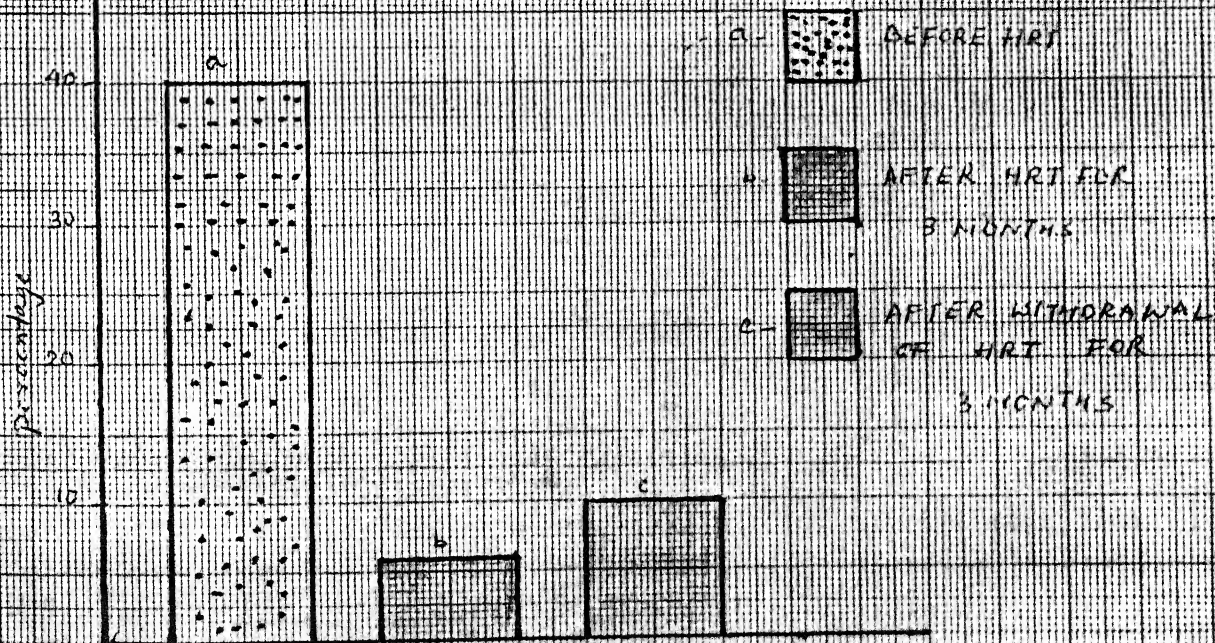
Graph showing serum total cholesterol values in individual patients before, after HRT and after withdrawal of HRT in Group A

mg/dl

patients

(•) → Before HRT
(●) → After HRT
(★) → After withdrawal of HRT
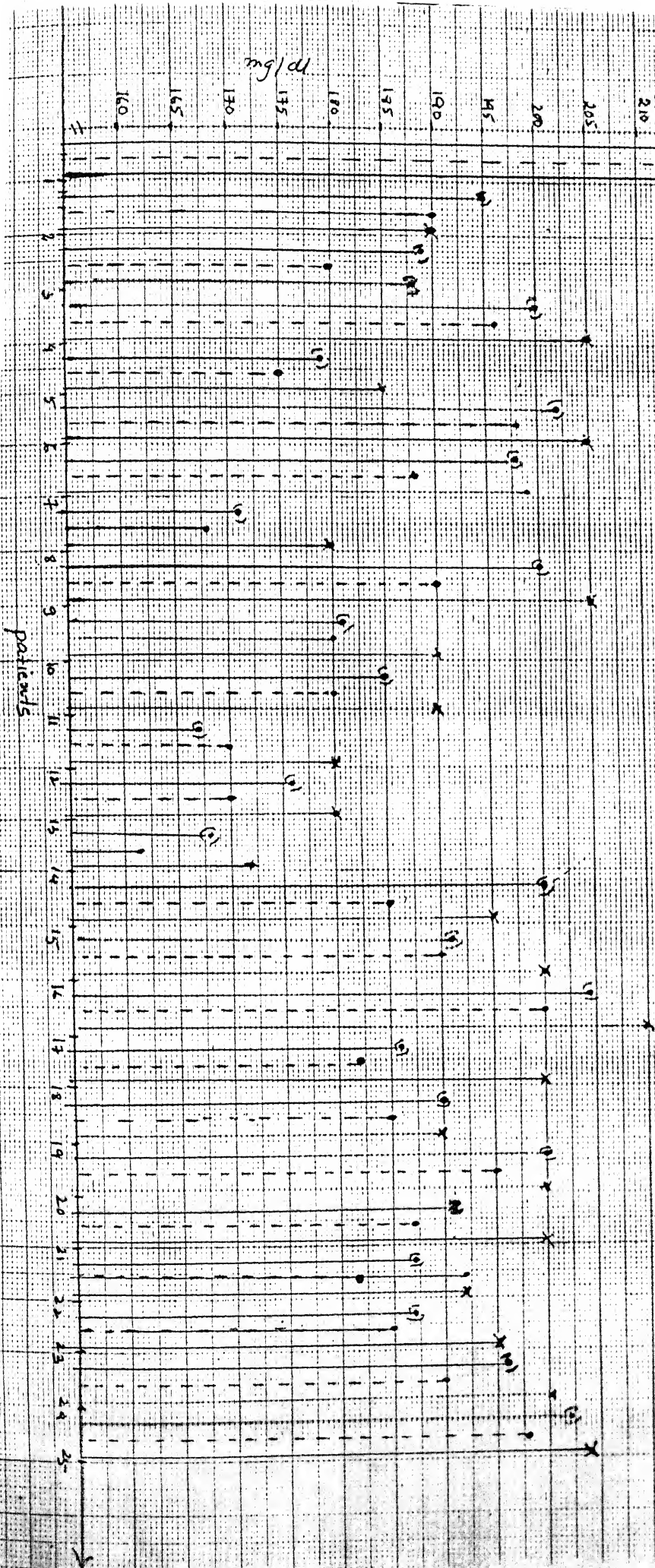
FALL IN LEVEL OF SERUM TRIGLYCERIDE AFTER TAKING H.R.T. FOR 3 MONTHS IN GROUP-A
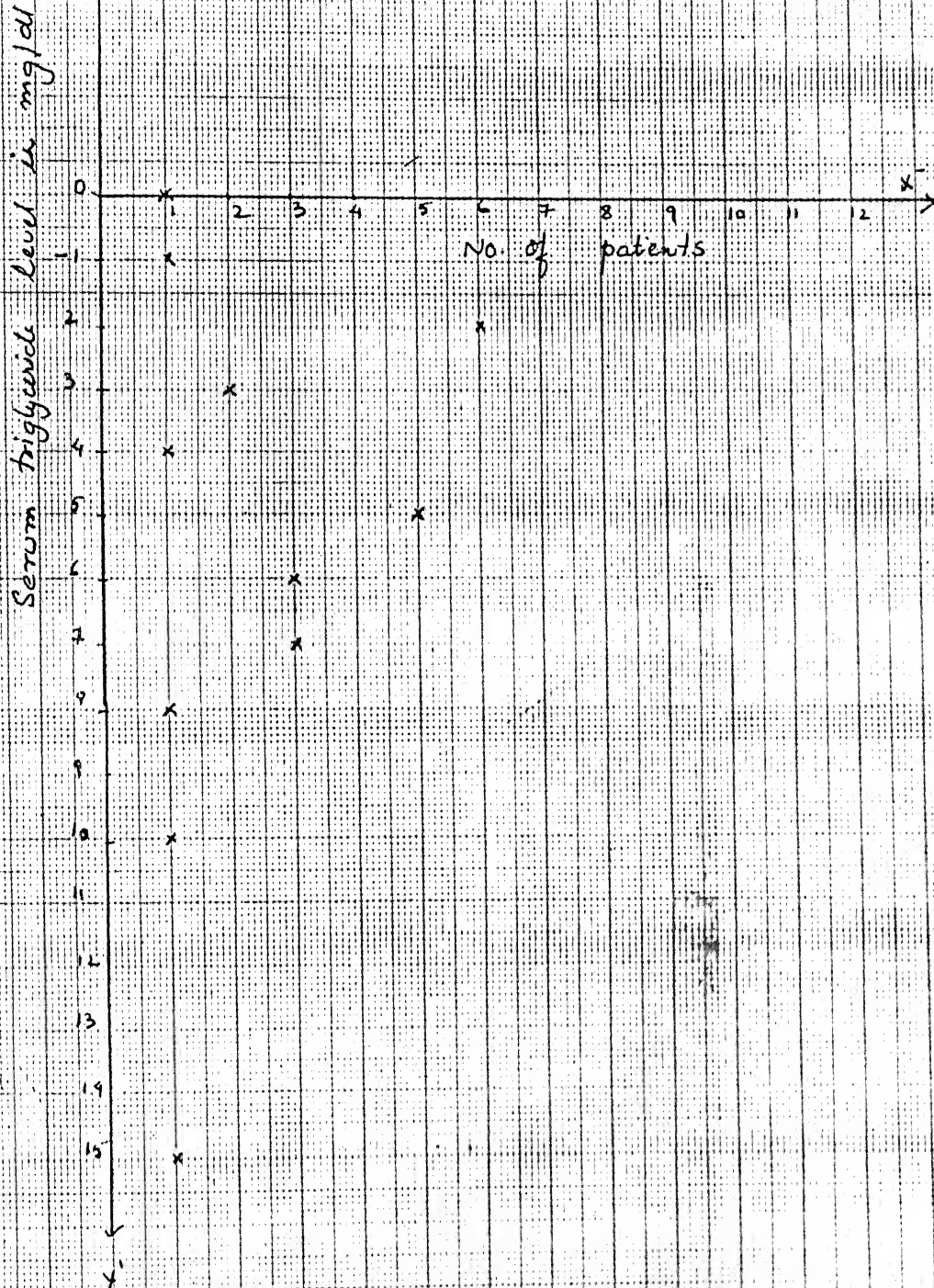
RISE IN LEVEL OF SERUM TRIGLYCERIDE LEVEL AFTER WITHDRAWAL OF H.R.T FOR 3 MONTHS IN GROUP- A

Serum triglyceride level in mg/dl

No. of Patients

Graph showing Rise in Level of low density lipoprotein in mg/dl in individual patients (group A) after stopping HRT for 3 months

LDL mg/dl

60
50
40
30
20
10

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25

Patients

Graph showing fall in level of very low density lipoprotein after taking H.R.T in Group. A patients.

V.L.D.L in mg/dl.

patients.

● → BEFORE H.R.T
× → AFTER H.R.T
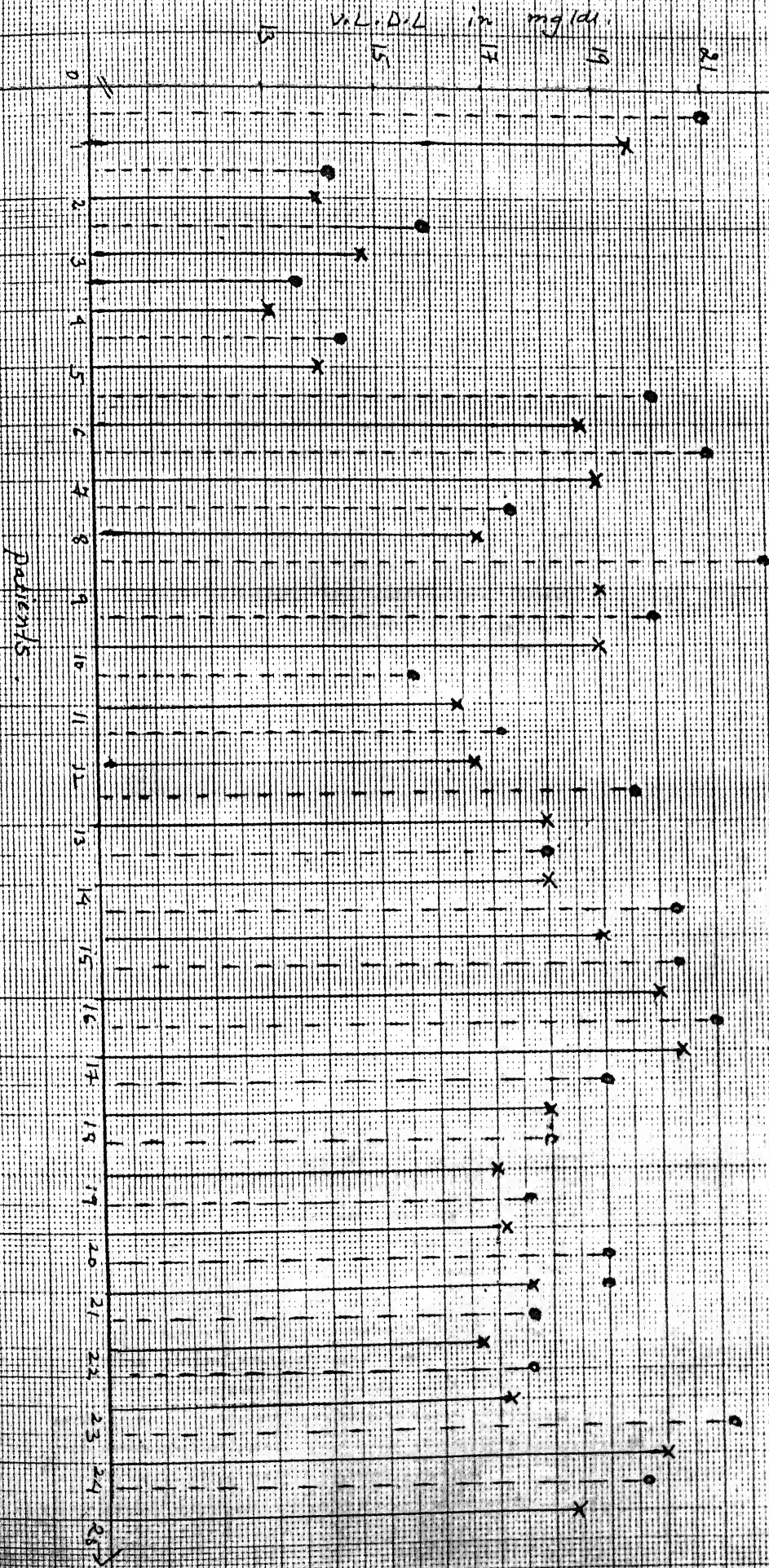
Graph showing rise in level of v.LDL
after withdrawal of H.RT in group A patients

● → After HRT
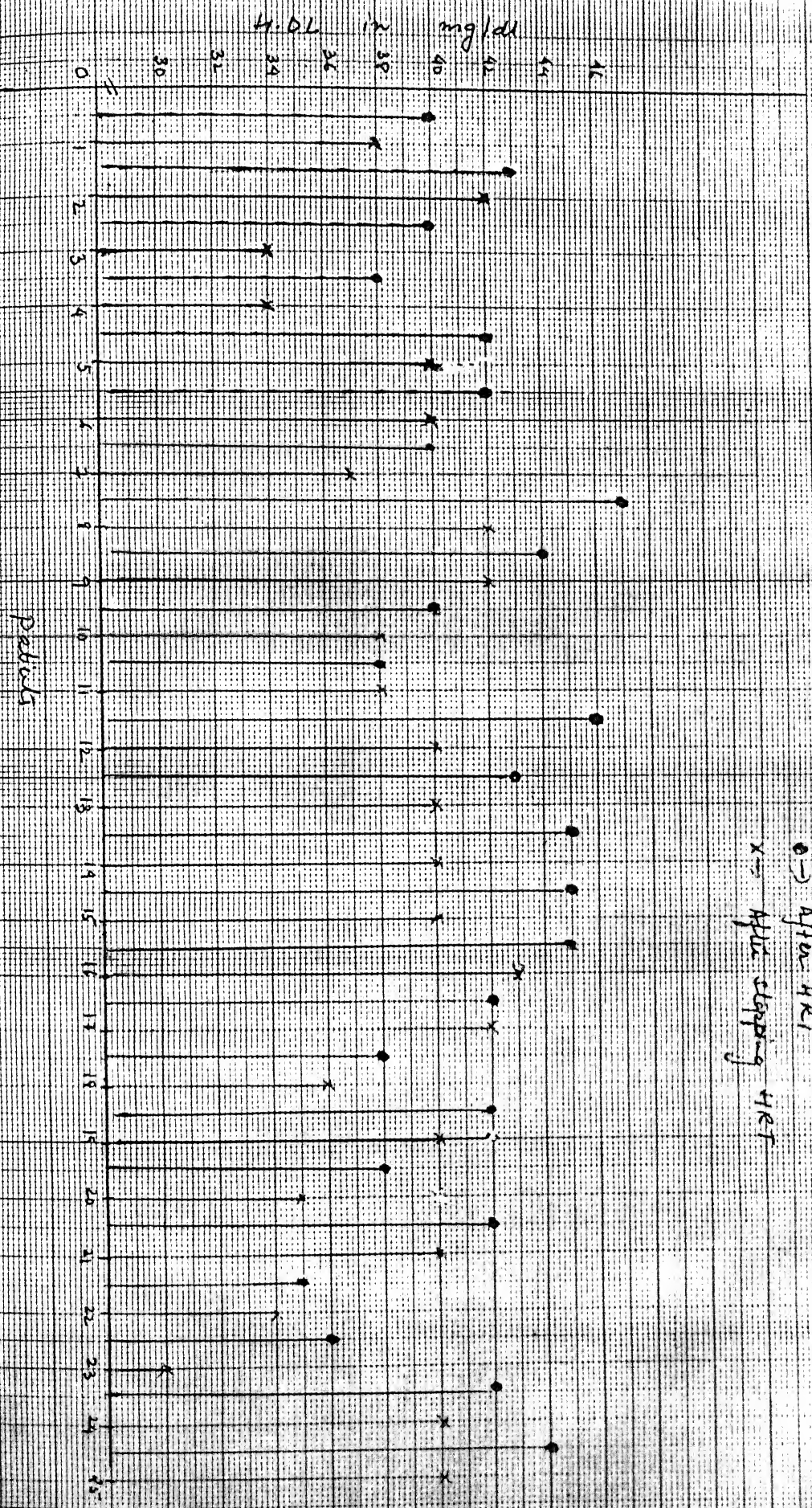✗ → After stopping HRT for 3 months

VLDL   mg/dl
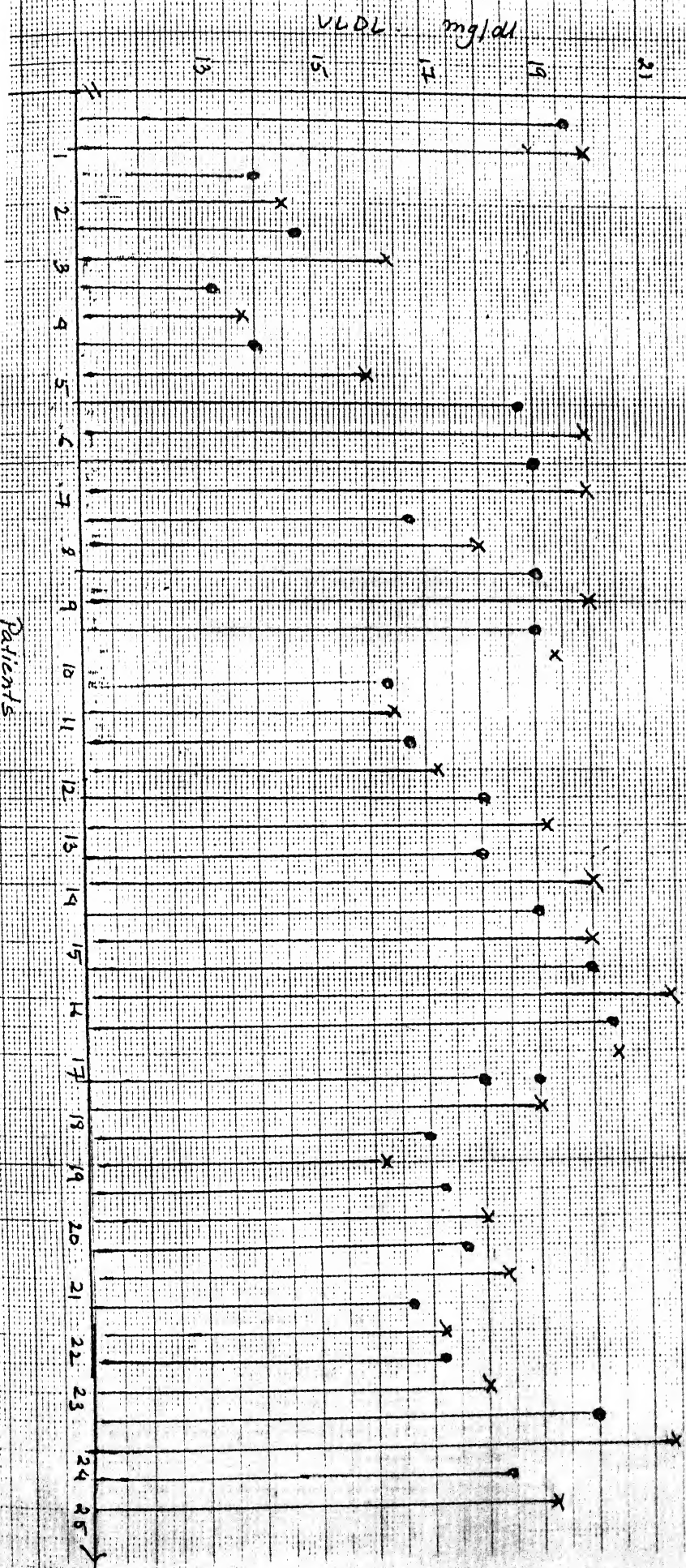
Patients

Graph showing level of high density lipoprotein in individual
patient before H.R.T and after taking H.R.T
for 3 months in group A patients
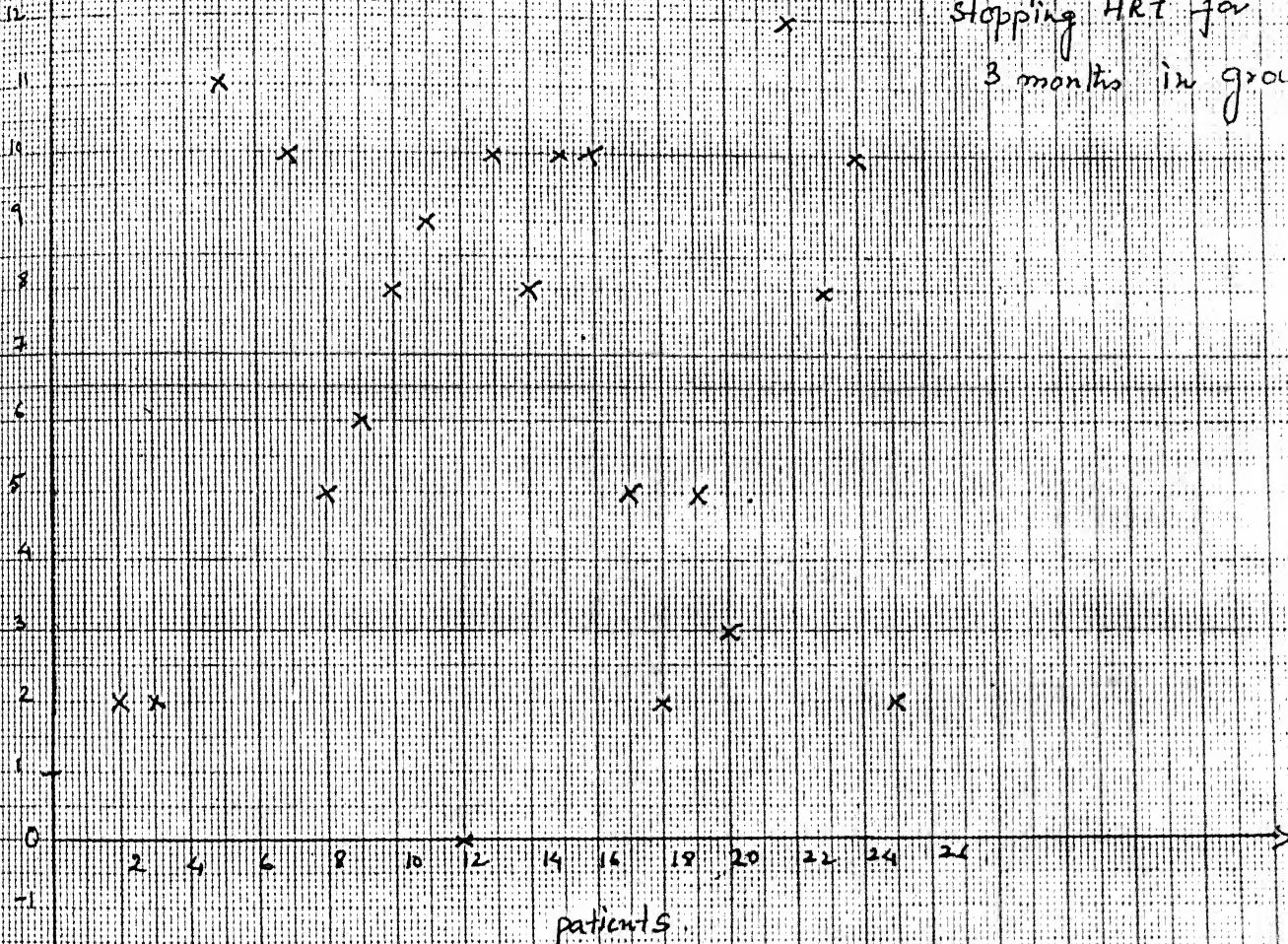
x → Before H.R.T
● After H.R.T

H.D.L level in mg/dl
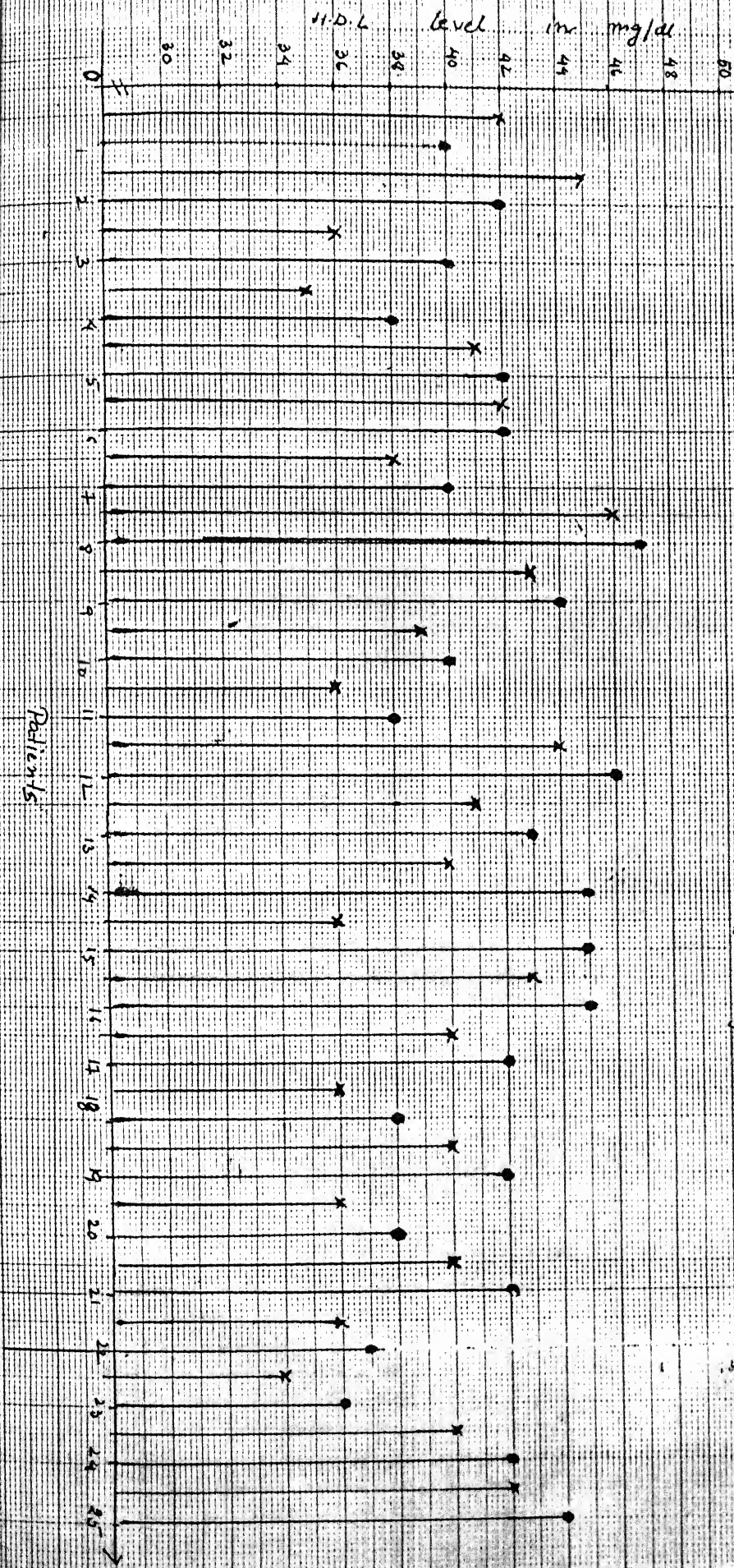
Patients

Graph showing level of high density lipoprotein in
individual patient after HRT and after stopping HRT
for 3 months in group A patients.
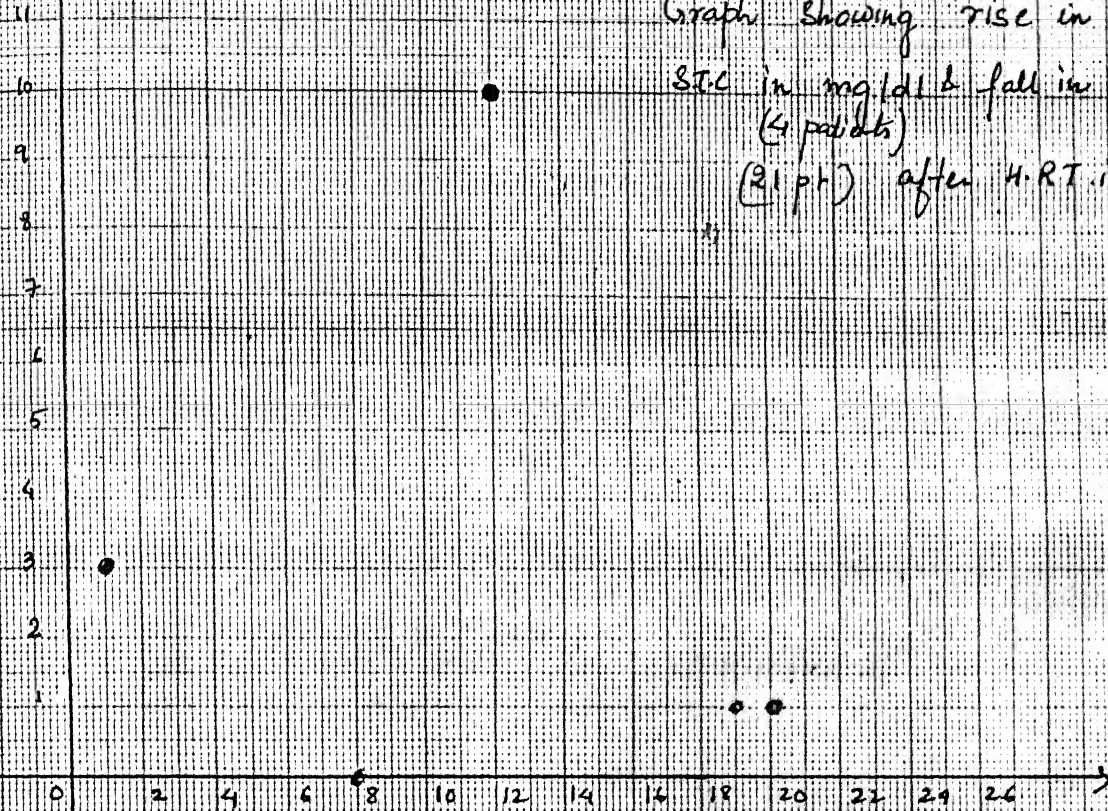
●—— After HRT
×—— After stopping HRT

HDL mg/dl

Graph showing rise in level of S.T.G in mg/dl in 22 patients and fall in level in STC level in 3 patients after stopping HRT for 3 months in group B
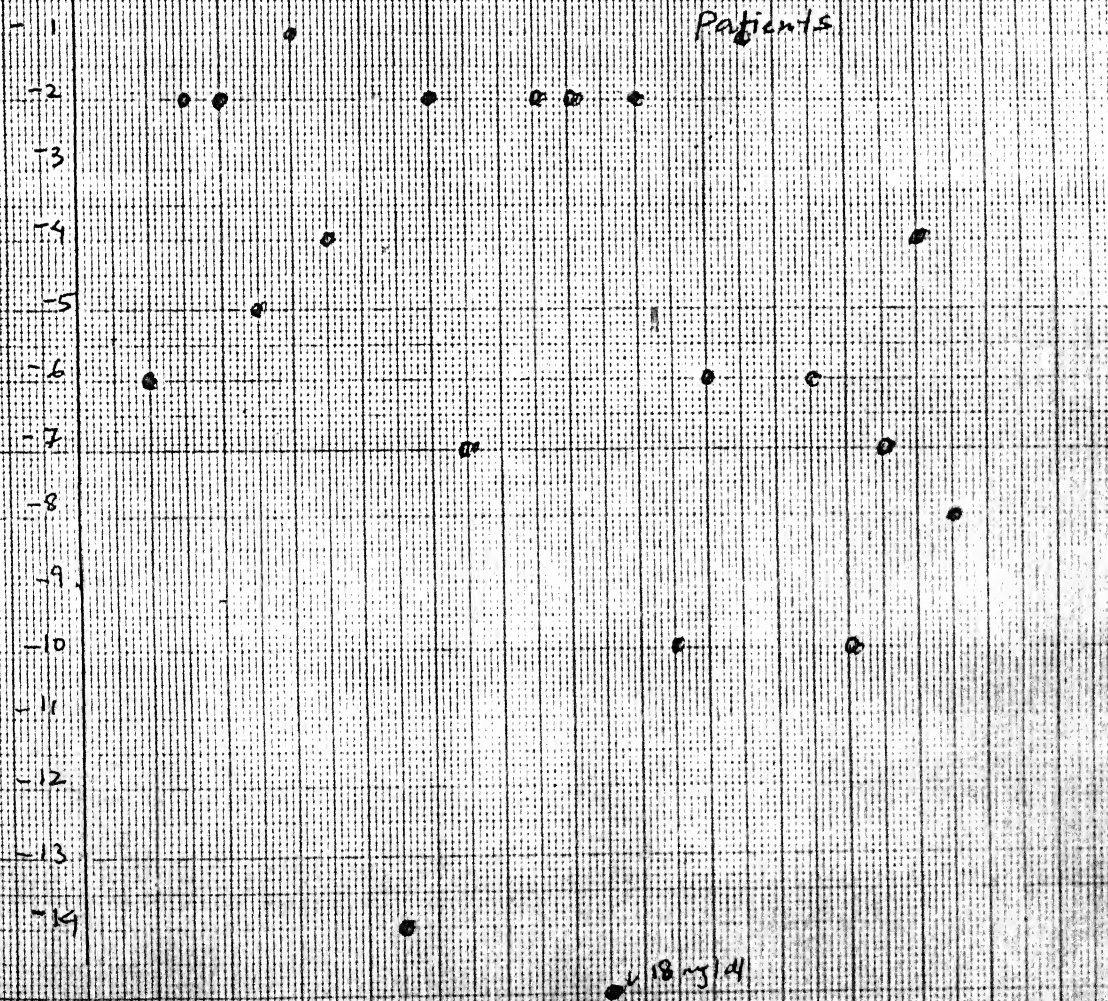
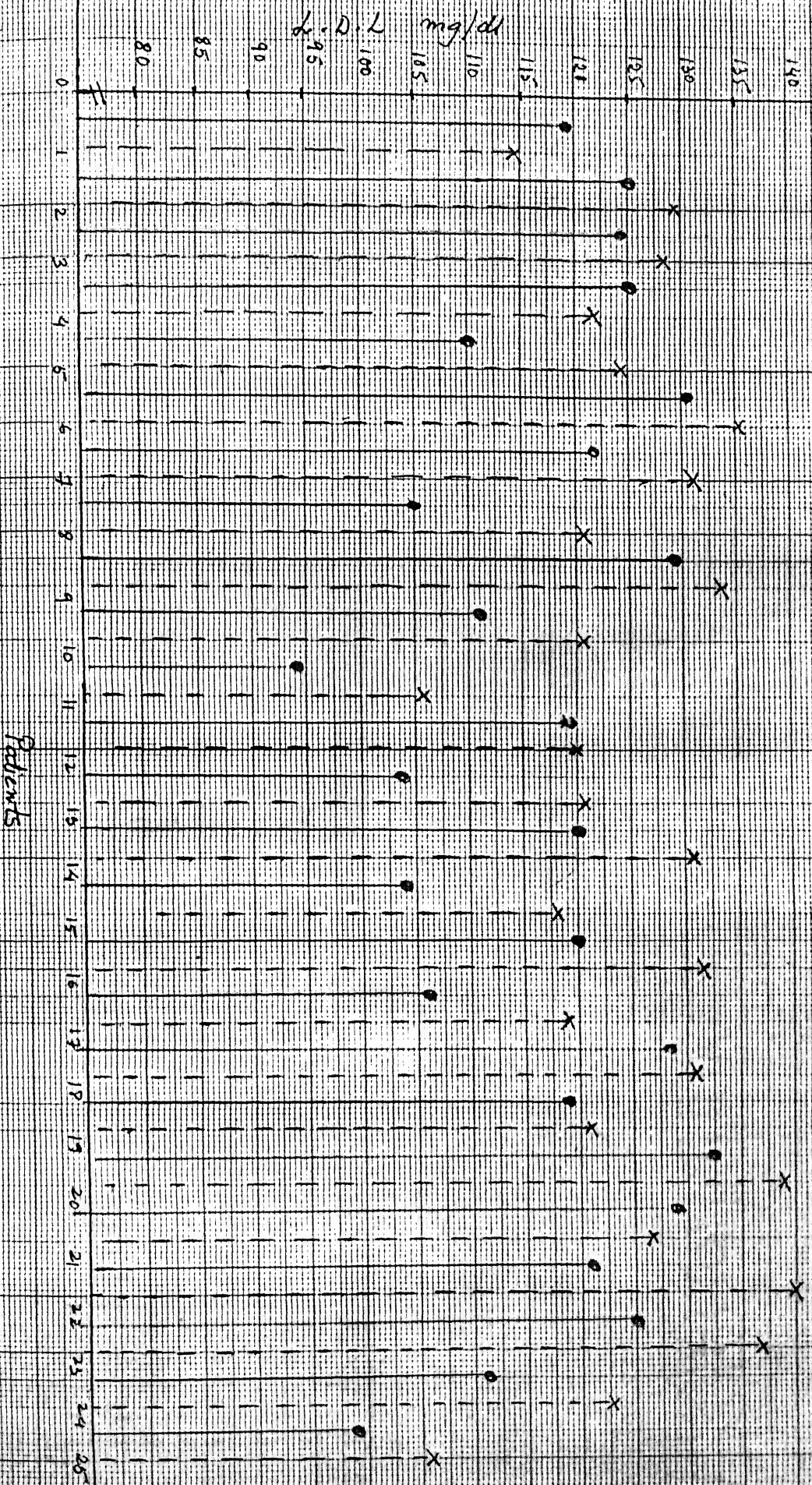Graph showing rise in level of STC in mg/dl & fall in STC level (4 patients) (21 pt.) after HRT in group B

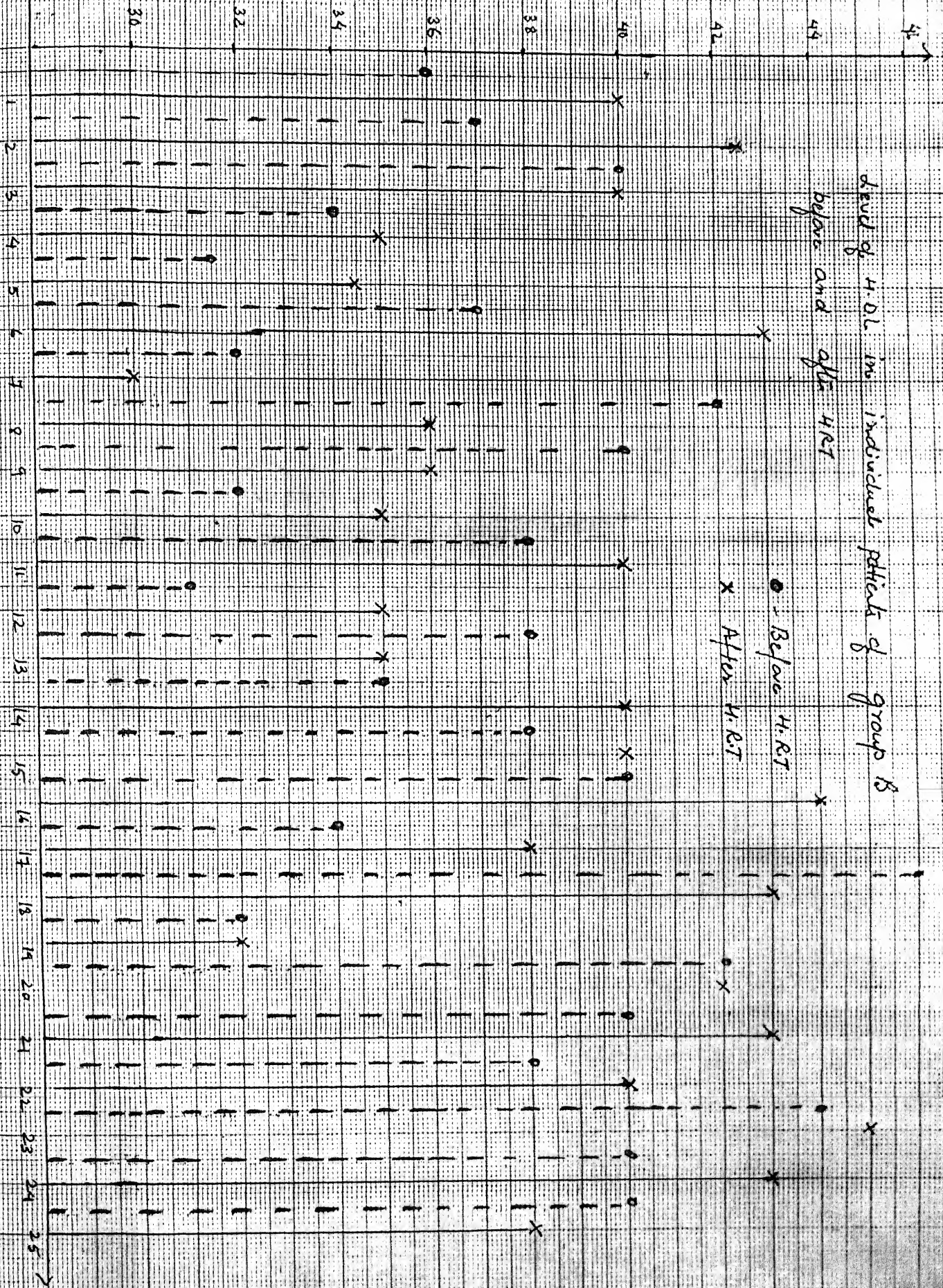graph showing mise the level of L.D.L level in individual patients after stopping H.RT in group B patients

L.D.L mg/dl

Patients

Level of H.D.L. in individual patients of group B before and after HRT

mg/dl

H.D.L.

● = Before H.R.T
× = After H.R.T

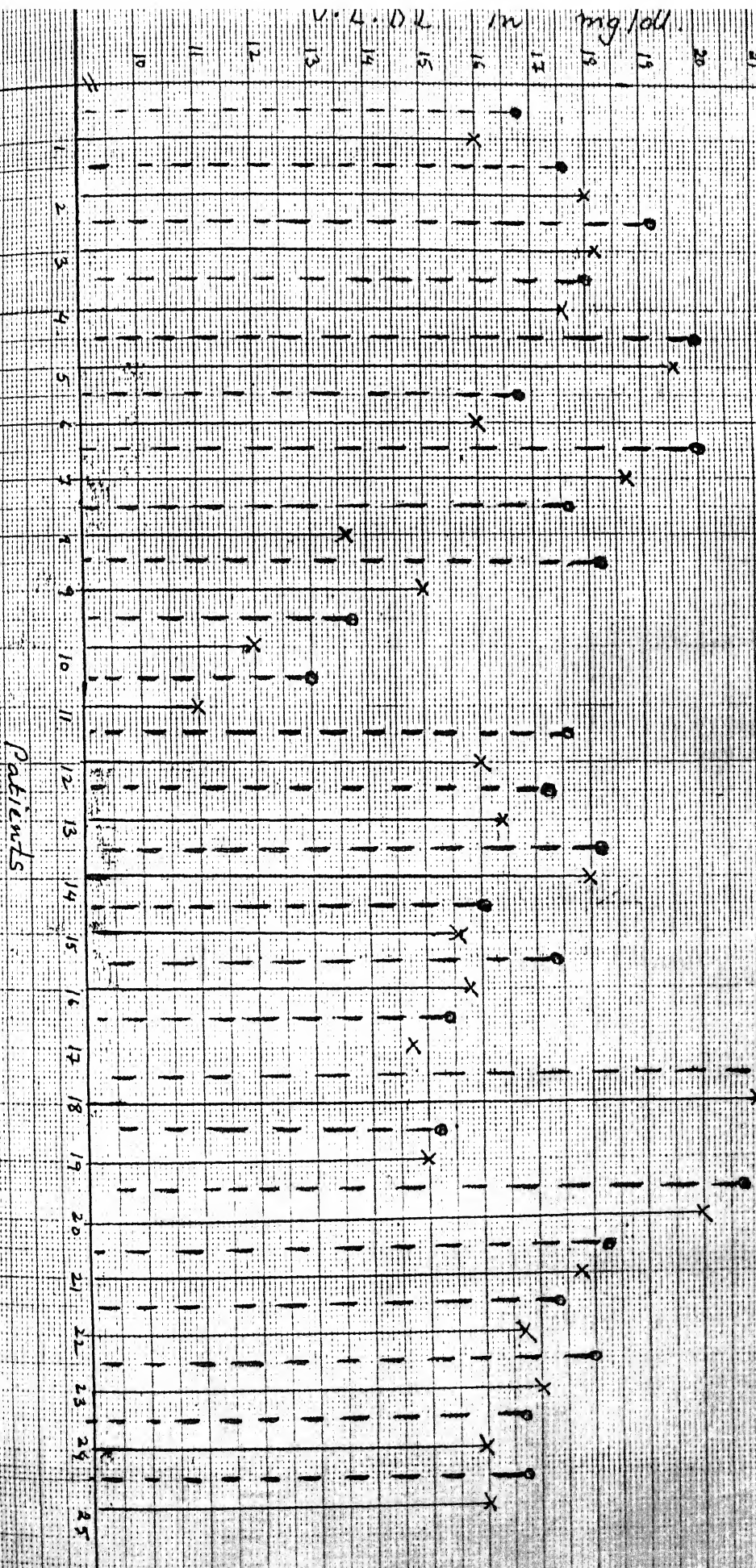Patients

Graph showing fall in level of H.D.L. after stopping H.R.T. for 3 months in Group B.
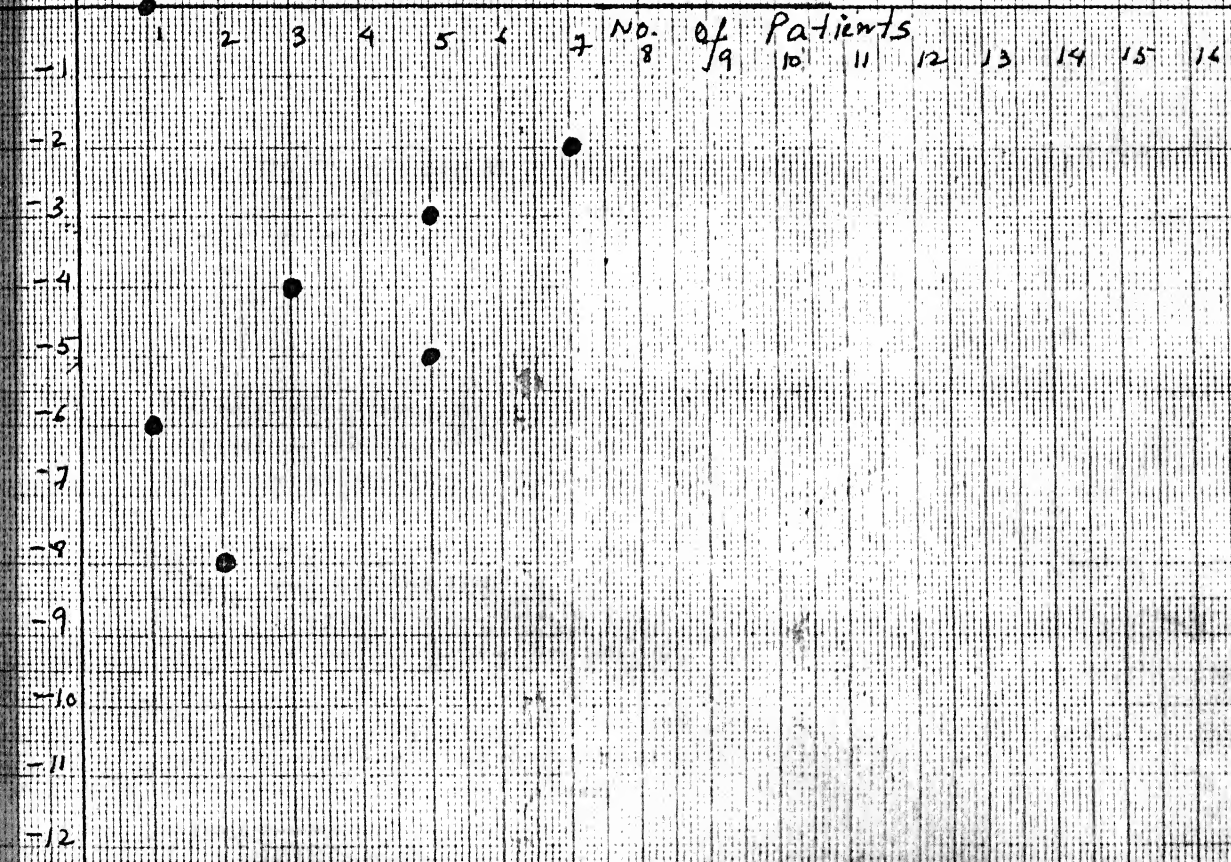
Graph showing fall in Vit.D.L. level after 4. RT in individual patients after taking 4. RT in group B.

mg/dl

Patients

Graph showing rise in STG in Group
B patients after stopping HRT for 3 months
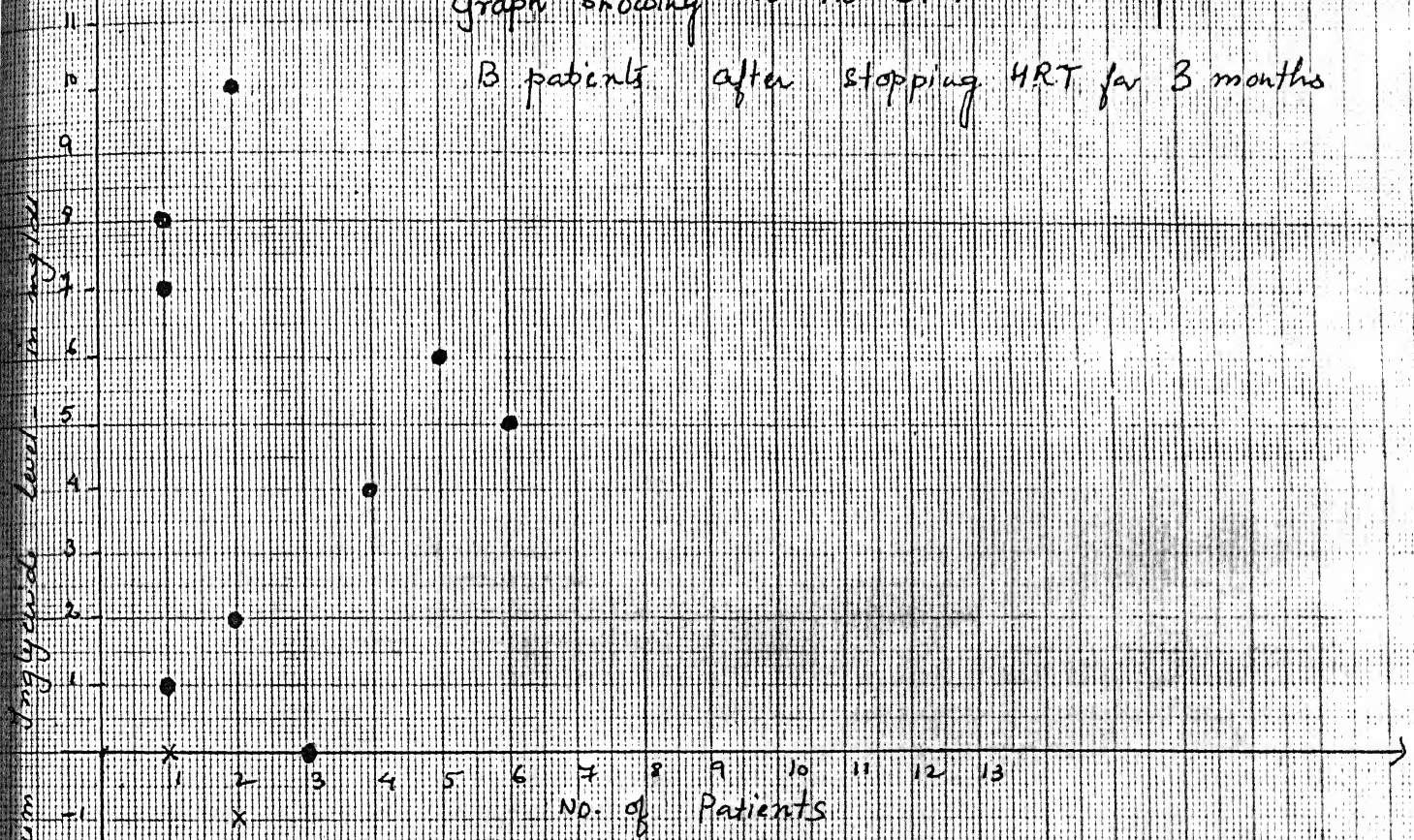
Graph showing fall in level of
STG level in group B patients
after H.R.T

LDL : HDL

4.60
4.40
4.20
4.00
3.80
3.60
3.40
3.20
3.00
2.80
2.60
2.40

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
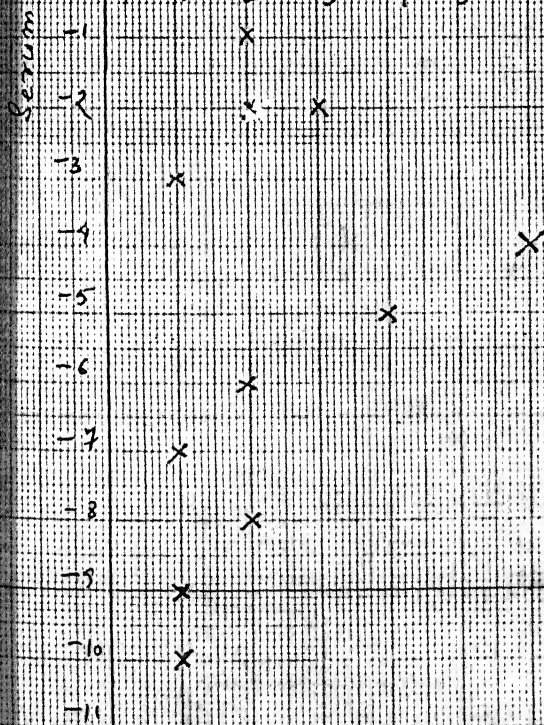
Patients

Graph showing values of LDL:HDL in individuals of group B before and after HRT
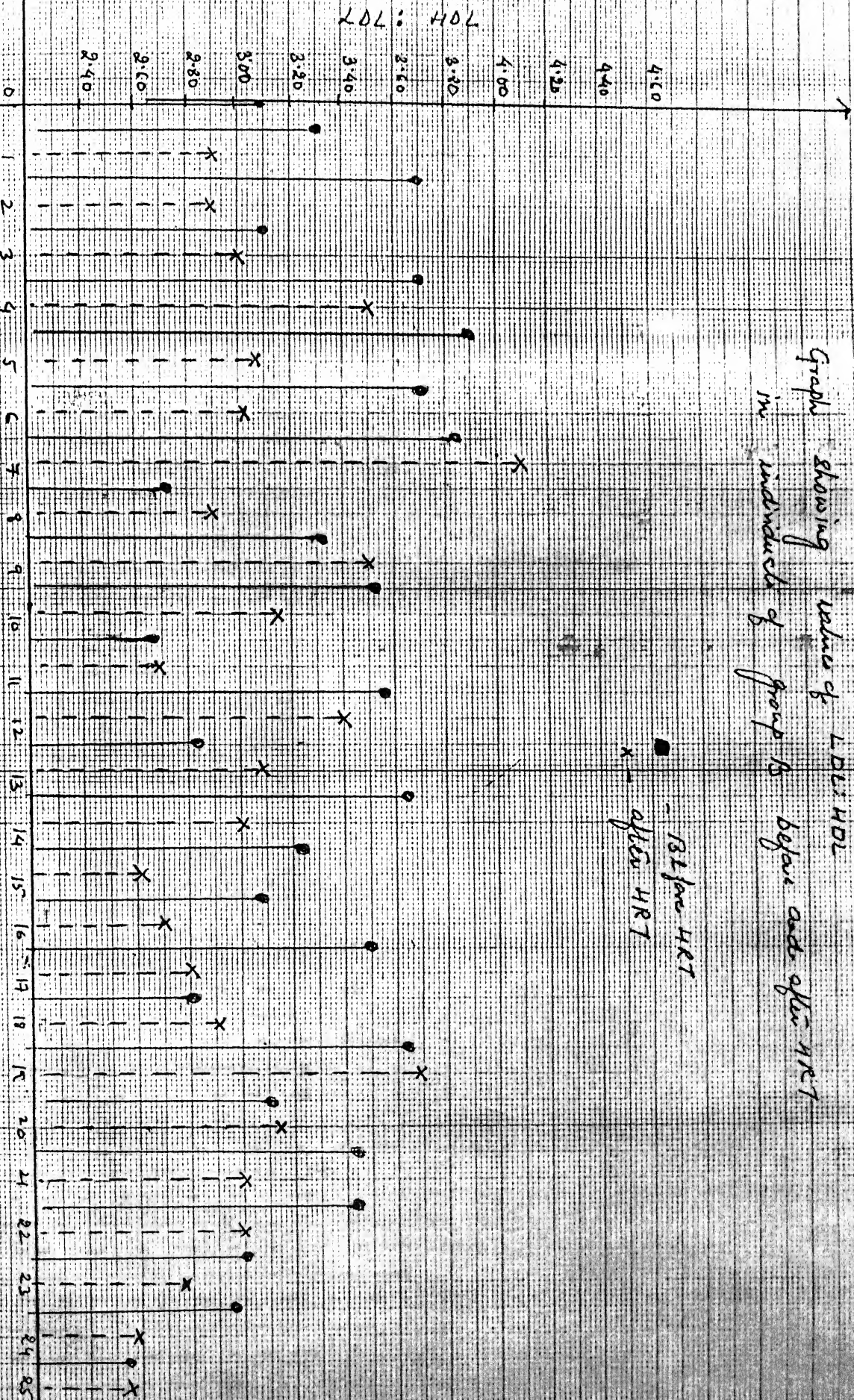
● — Before HRT
x — after HRT

Graph showing Ratio of LDL & HDL in individual patients of group A before and after HRT

LDL: HDL

● — Before H.R.T

✕ — After H.R.T
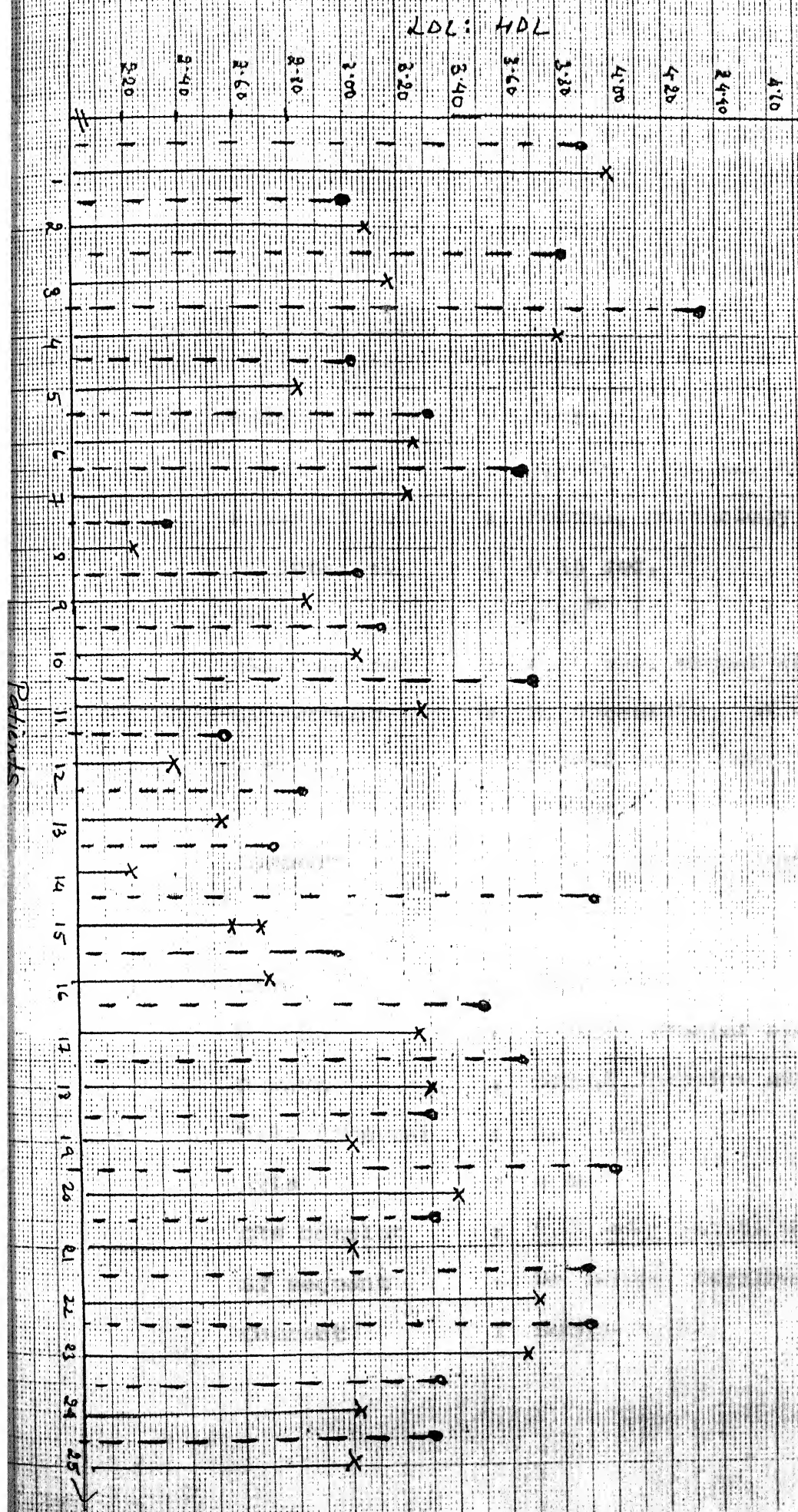
Patients

After withdrawal of HRT, 5 patients had vaginal discharge and after cytology examination they showed dominance of basal cells.

E.C.G. RECORDING

Group A : Before taking HRT

1. Name   : Hazra
   P.R.   : 72/min, regular, sinus rhythm
   P wave   : Normal, morphology and duration
   PR interval   : 0.16 sec.
   Axis   : + 60°
   QRS complex   : 0.10 sec. normal configuration.
   ST segment   : No depression, no coving & elevation.
   T wave   : Normal configuration
   U wave   : absent
   Comment   : Within normal limit.

2. Name   : Chiya Rani
   P rate   : 72/min, regular sinus rhythm
   P wave   : Normal duration and morphology.
   P.R. interval   : 0.12 sec.
   Axis   : + 60°
   QRS complex   : 0.08 sec, normal configuration
   ST segment   : No coving, depression or elevation.
   Comment   : Normal E.C.G.

kneet

kneet

kneet
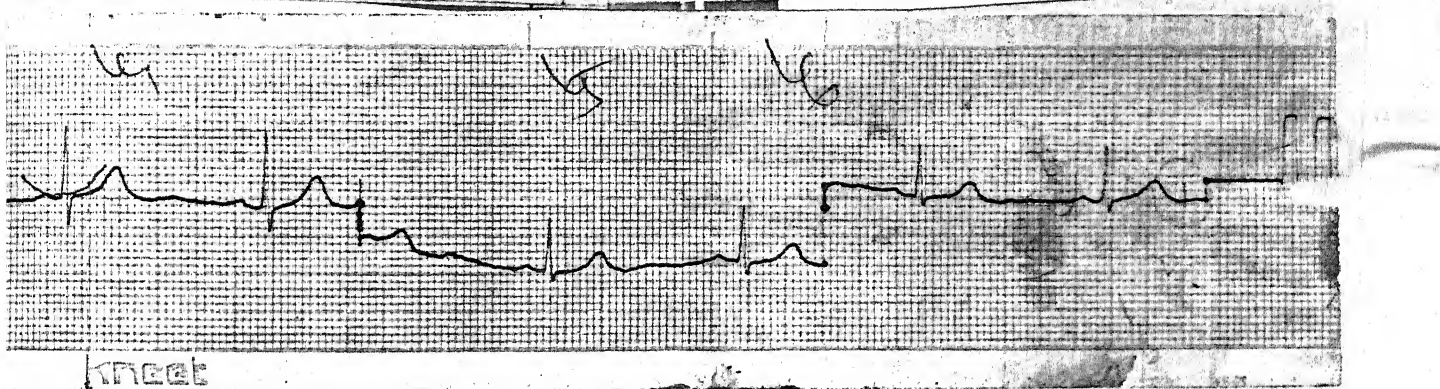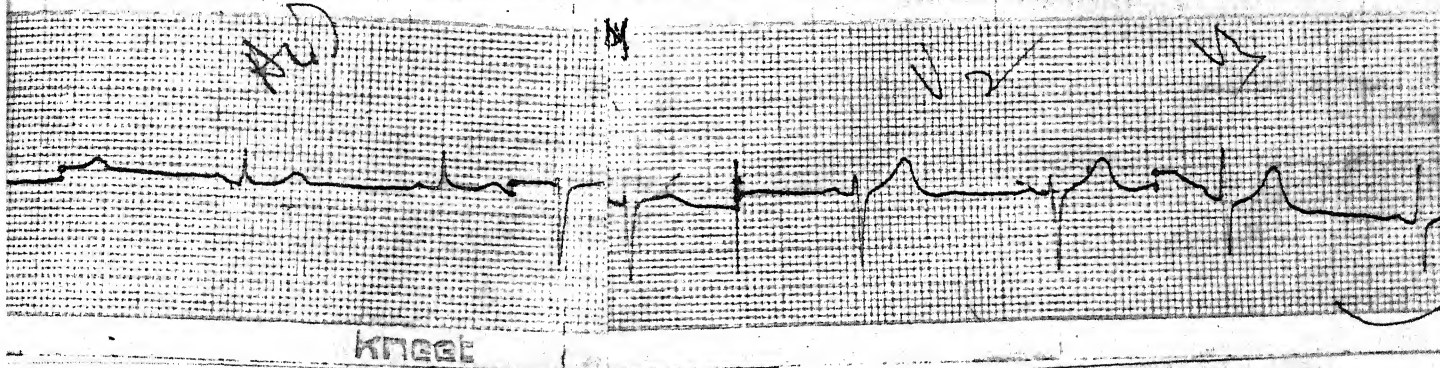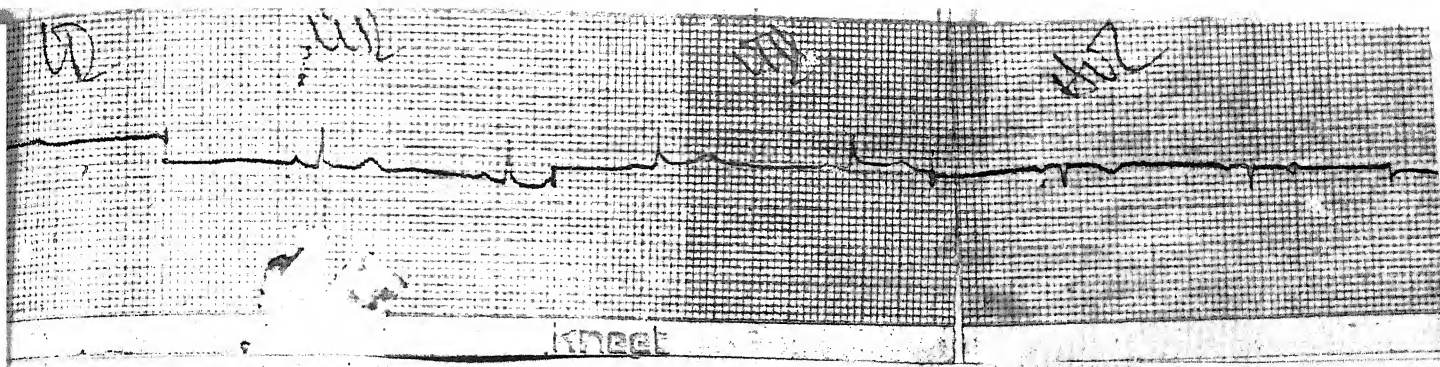
HAZRA
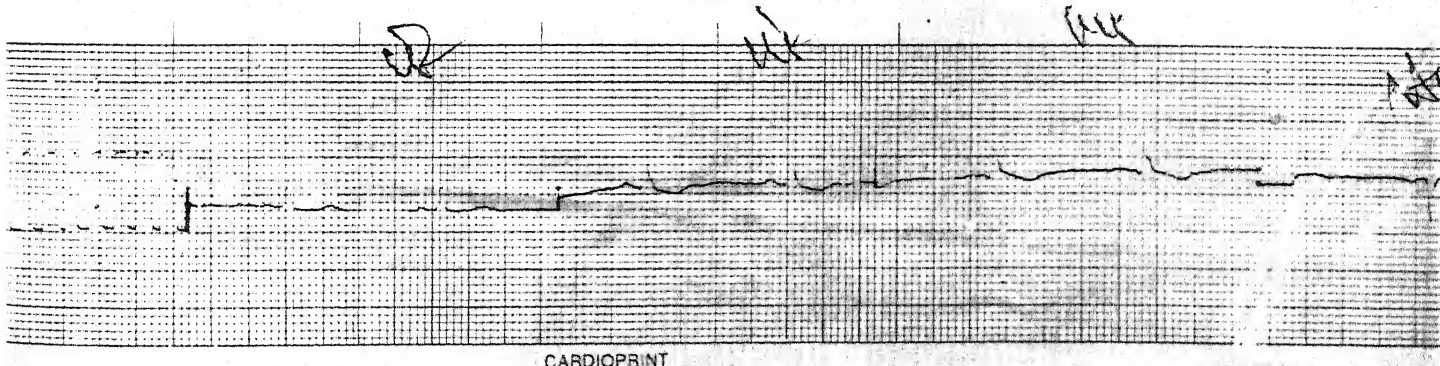
CARDIOPRINT
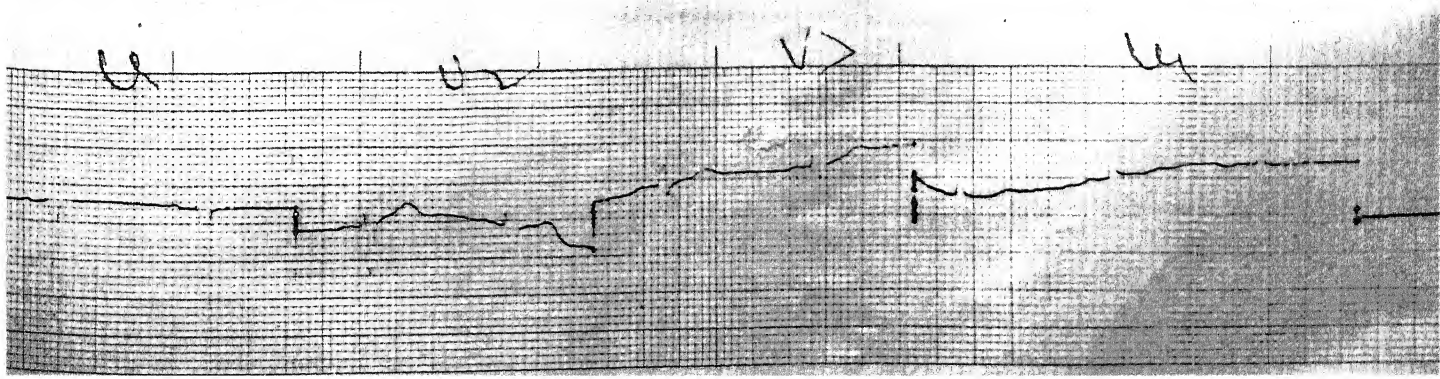
3. Name : Dropadi

    P. rate : 80/min. regular sinus rhythm

    P wave : Normal duration and morphology

    PR interval : 0.20 sec.

    Axis : +30°

    QRS complex : 0.12 sec. normal configuration

    ST segment : No coving, no elevation present.

    T wave : Normal configuration

    Comment : Within normal limit.

4. Name : Manju

    P. rate : 68/min. regular sinus rhythm.

    P wave : Normal morphology and duration

    PR interval : 0.16 sec.

    Axis : + 75°

    QRS complex : 0.08 sec. normal configuration.

    ST segment : No depression, coving or elevation.

    T wave : Normal configuration.

    Comment : Normal E.C.G.

I   AVF

V6

Orcpdi

AVF

V5   V6
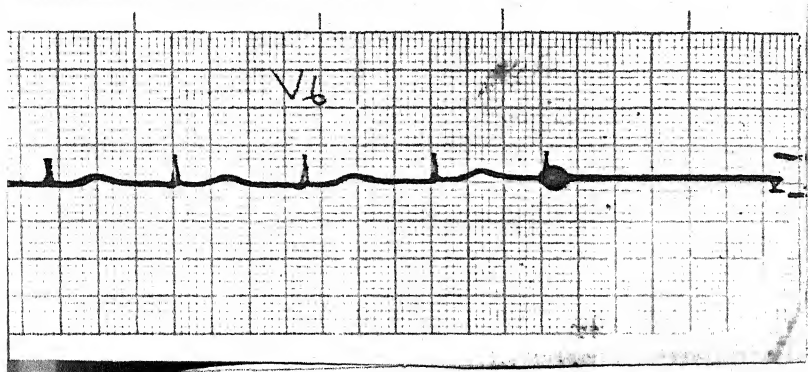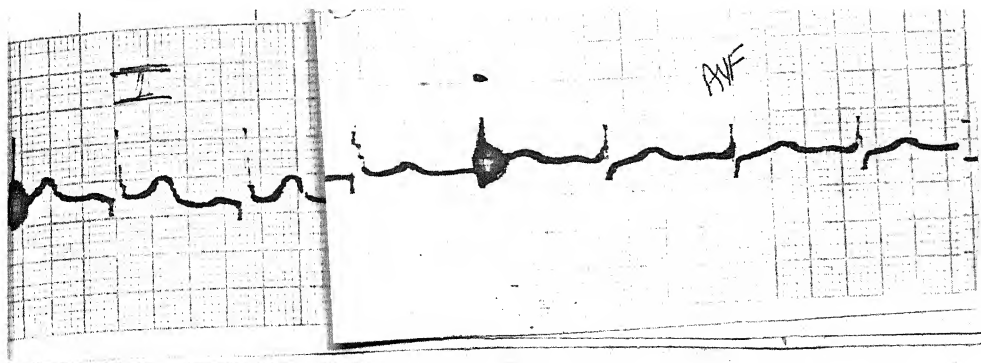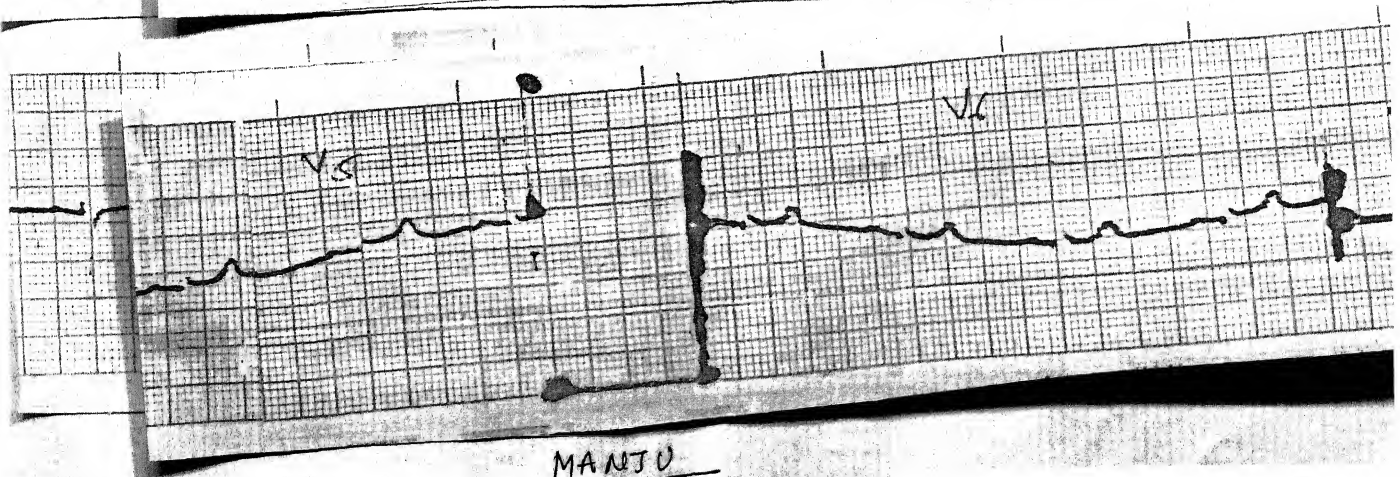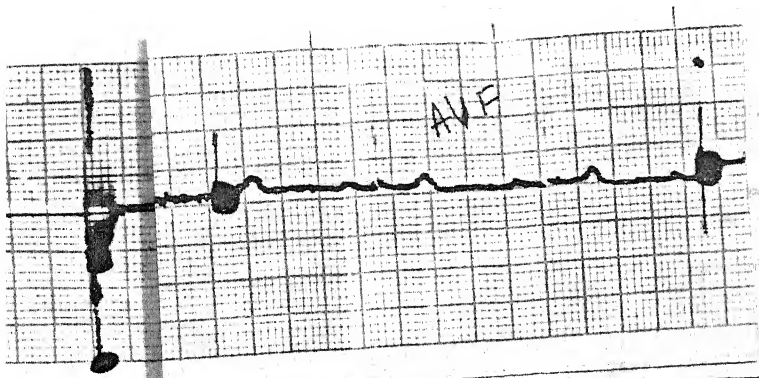
MANJU

5.   Name   : Munni

     P. rate   : 75/min, normal sinus rhythm

     P wave   : Normal morphology and duration

     Axis   : + 45°

     QRS complex   : 0.08 second, Normal morphology and
                        duration.

     ST segment   : No coving, no depression,
                        no elevation.

     T wave   : Normal morphology

     U wave   : Absent

     Comment   : Normal E.C.G.

6.   Name   : Bhagwati

     P. rate   : 75/min, regular sinus rhythm

     P wave   : Normal duration & morphology

     PR interval   : 0.16 sec

     Axis   : +30°

     QRS complex   : 0.08 sec.

     ST segment   : One segment ST depression in
                        II, III, aVf.

     T wave   : Normal configuration

     Comment   : Within normal limit
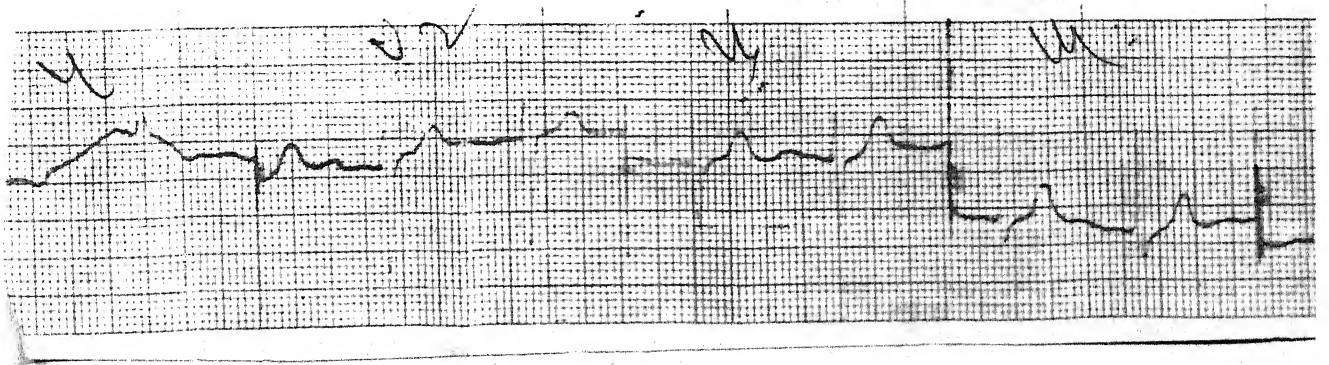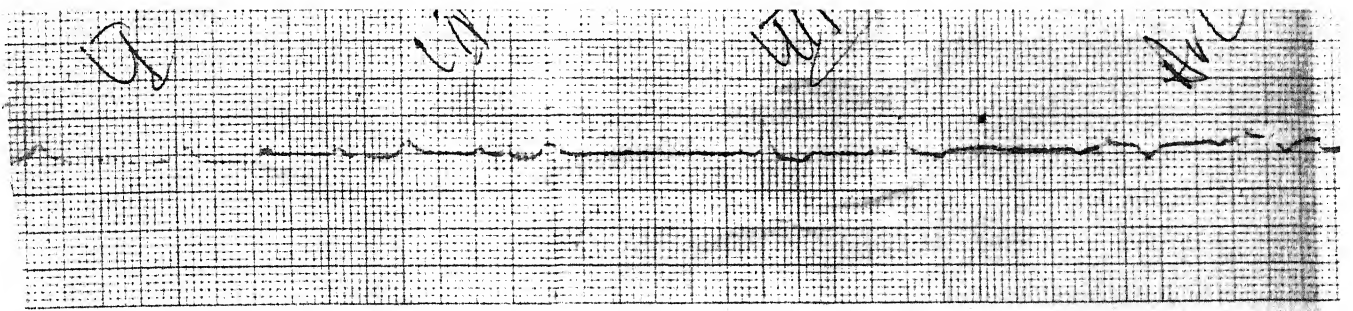
MUNNI
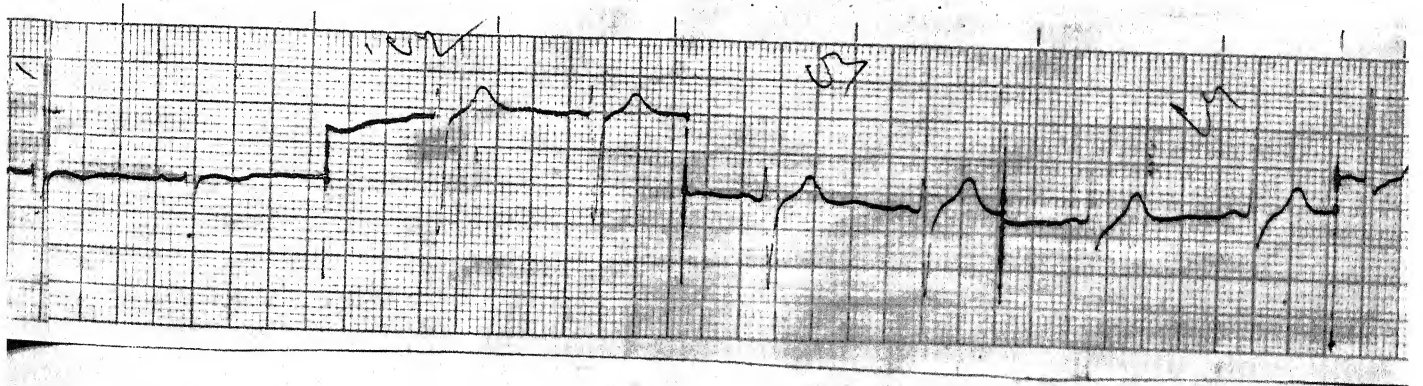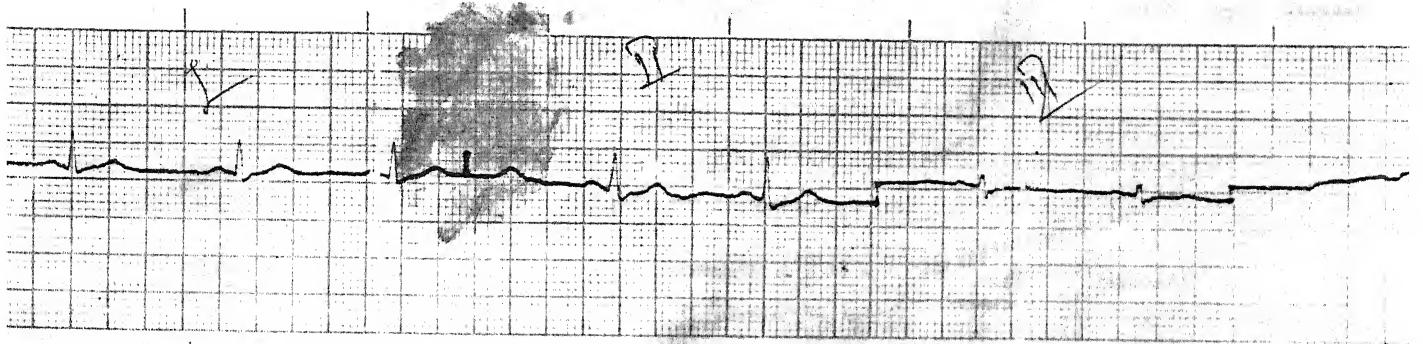
Bhagwati

7. Name   : Kasturi

  P. rate   : 72/min, regular sinus rhythm

  P wave   : Normal duration & morphology

  Axis   : +60°

  QRS complex : 0.08 sec, no depression

  ST segment : No coving, no depression.

  T wave   : Normal morphology

  Comment   : Normal E.C.G.

8. Name   : Premwati

  P. rate   : 75/min, regular sinus rhythm

  P wave   : Normal morphology and duration

  Axis   : + 50°

  QRS complex : 0.08 sec, normal morphology and duration.

  ST segment : No elevation, no depression

  T wave   : Normal morphology

  Comment   : Within normal limit.
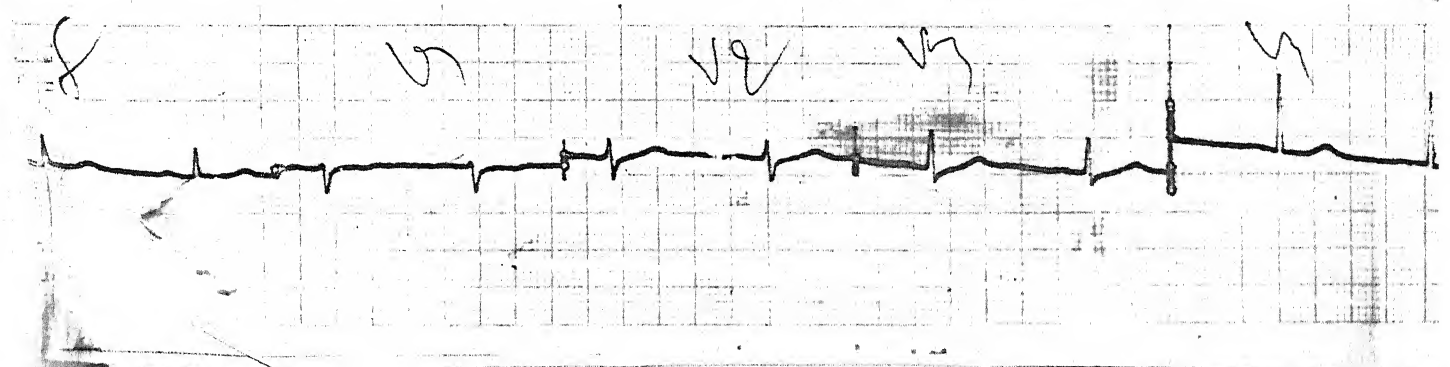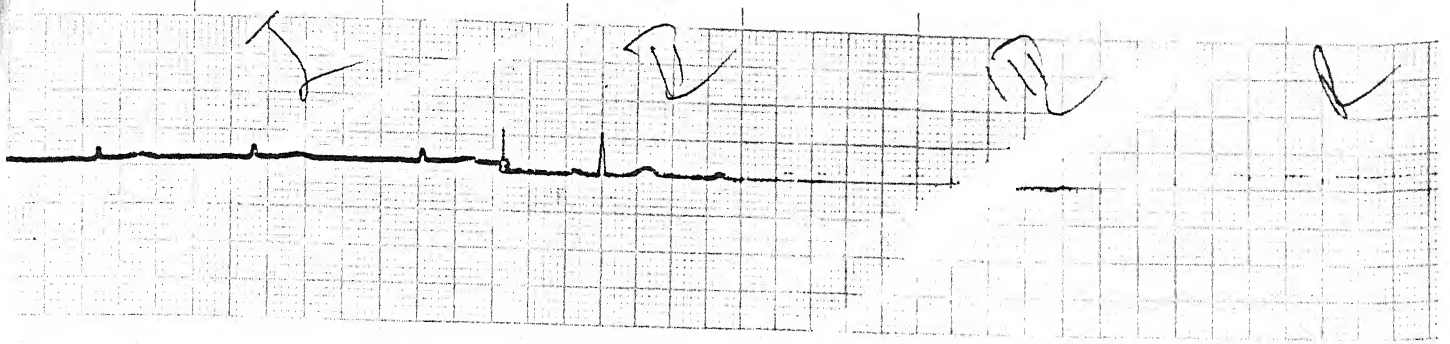
kastoori
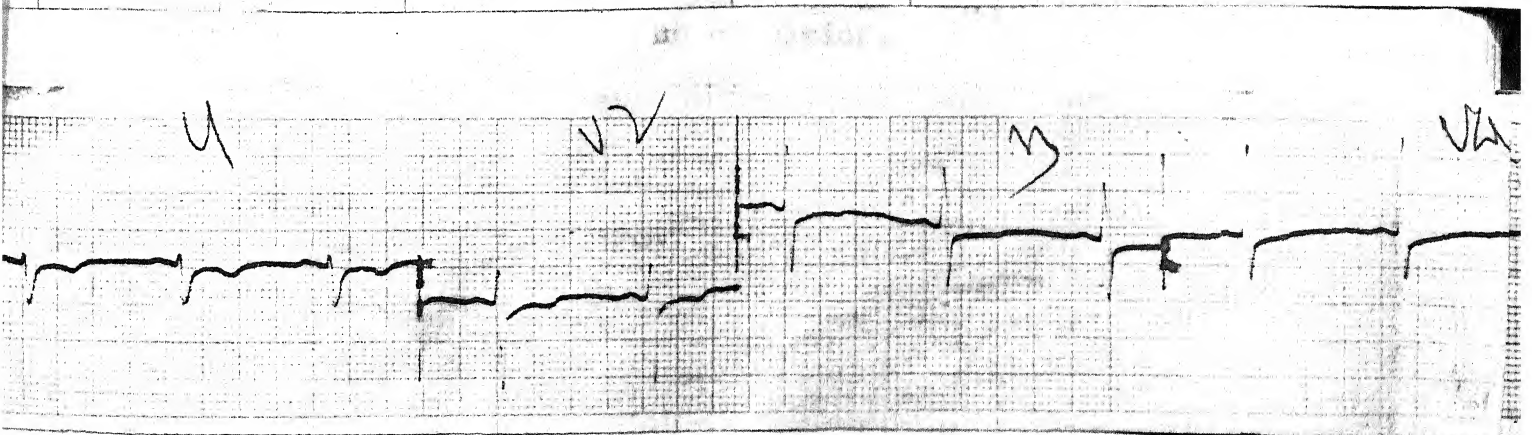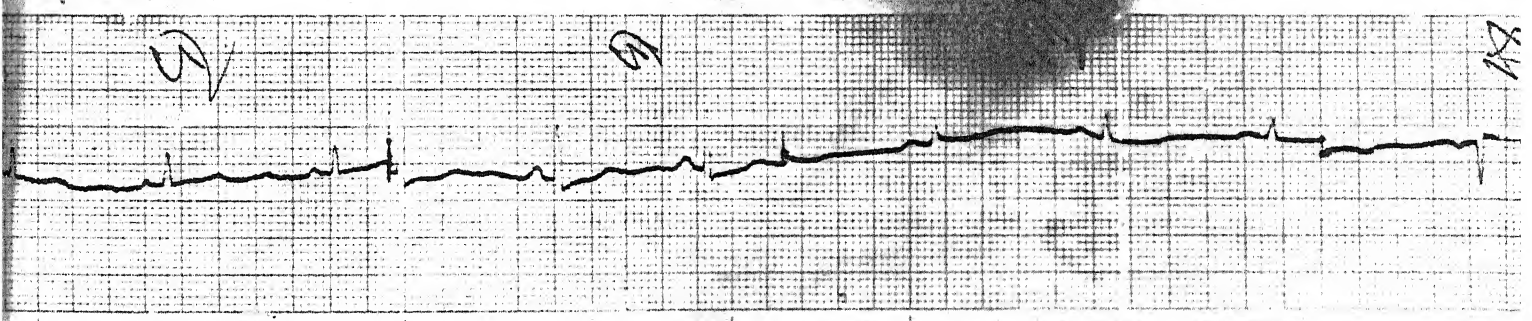
Premwati

9.   Name   :   Bhavni Bai

       P. rate   :   32/min, regular sinus rhythm

       P wave   :   Normal morphology & duration

       Axis   : $- 45^{\circ}$

       QRS complex   :   0.08 sec, normal morphology and duration.

       T wave   :   Normal morphology

       U wave   :   Absent

       Comment   :   Left axis deviation.

10.   Name   :   Laxmi

       P. rate   :   72/min

       P wave   :   Normal morphology & duration

       Axis   : $+ 30^{\circ}$

       QRS complex   :   0.08 sec, normal morphology

       ST segment   :   No coving, no depression, no elevation.

       Comment   :   Within normal limit.

Bhavni Sai
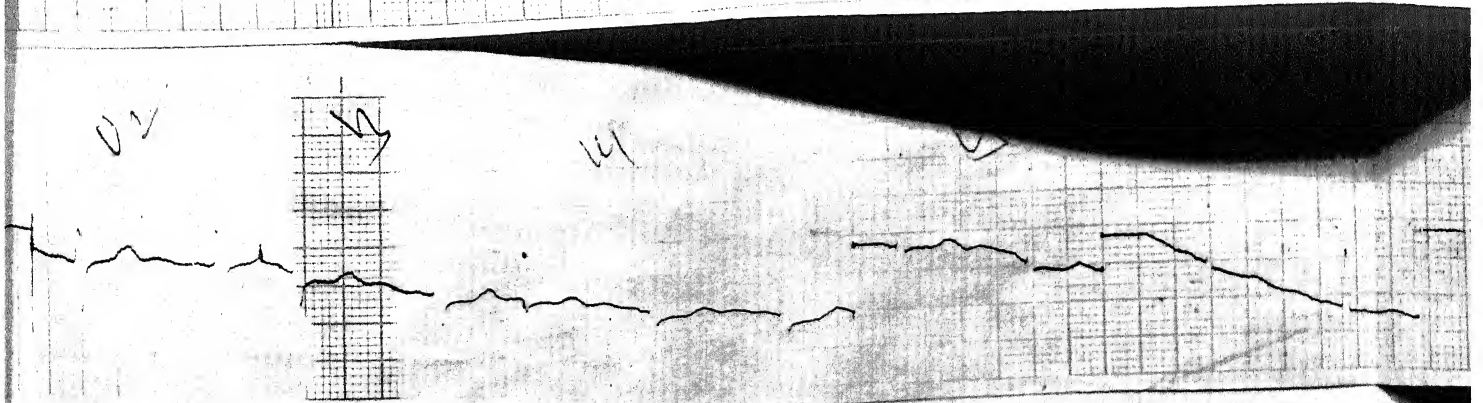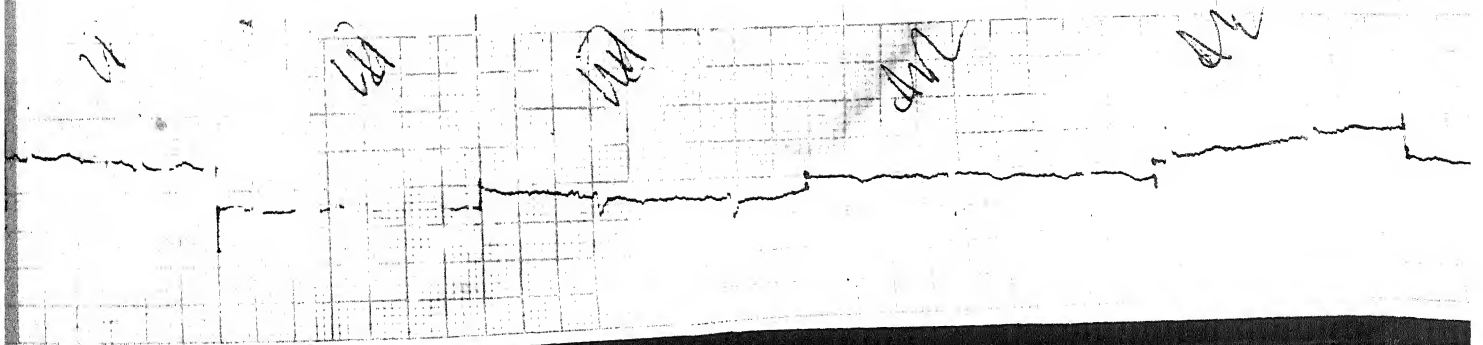
Laxmi

<u>After taking HRT for 3 months</u>

11. Name   **:** Janak Kishori

  P. rate   **:** 68/min, sinus rhythm

  P wave   **:** Normal morphology and duration

  Axis   **:** + 45°

  QRS complex **:** 0.12 sec, normal configuration

  ST segment **:** No coving, no depression, no elevation.

  T wave   **:** Normal morphology

  Comment **:** Normal E.C.G.

12. Name   **:** Kalpana

  P. rate   **:** 136/min, regular sinus rhythm

  P wave   **:** Normal morphology & duration

  Axis   **:** + 40°

  QRS complex **:** 0.08 sec, normal morphology, and normal duration.

  ST segment **:** No elevation, no depression

  T wave   **:** Normal morphology

  Comment **:** Sinus tachycardia
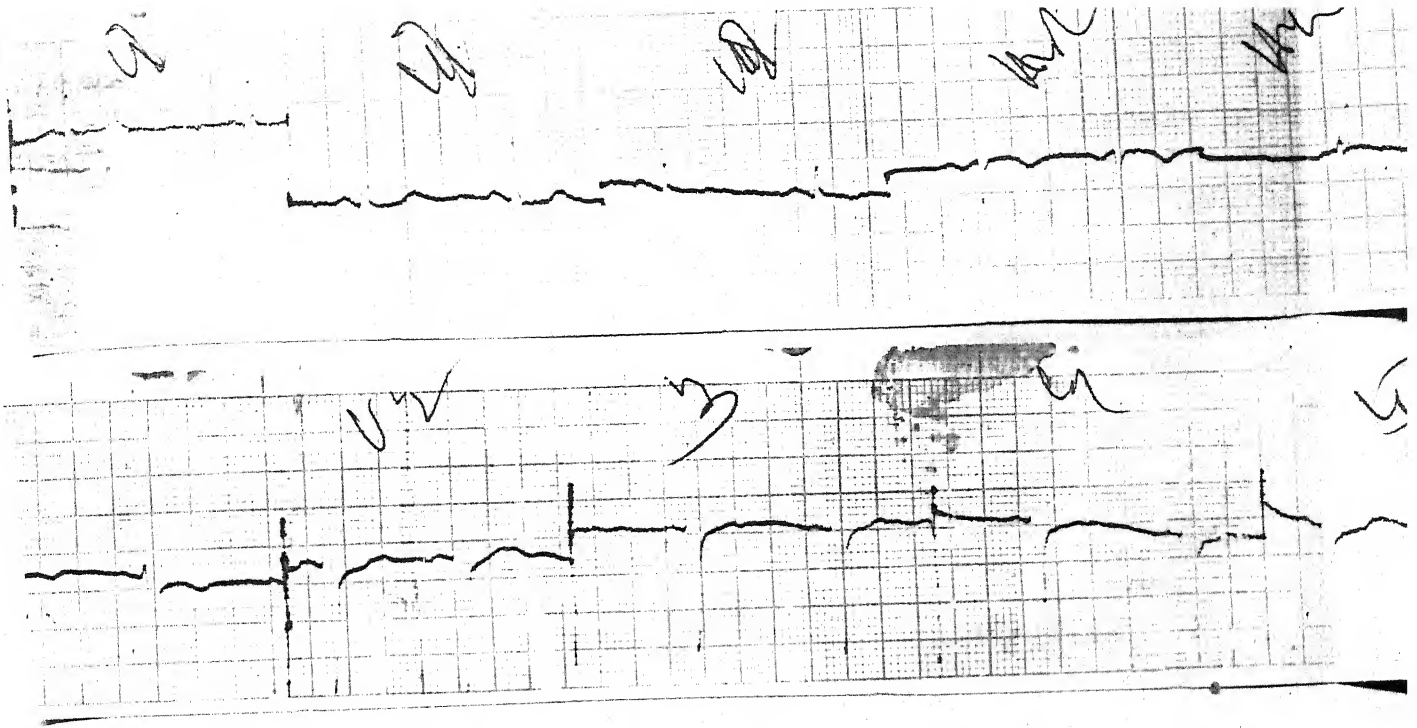
Janak Kishori
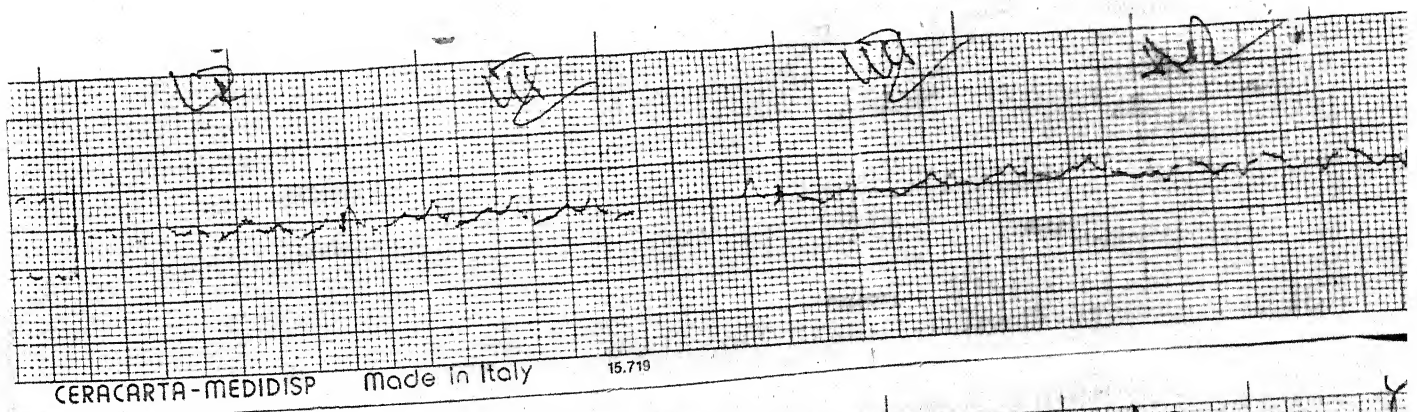
CERACARTA-MEDIDISP   Made in Italy   15.719
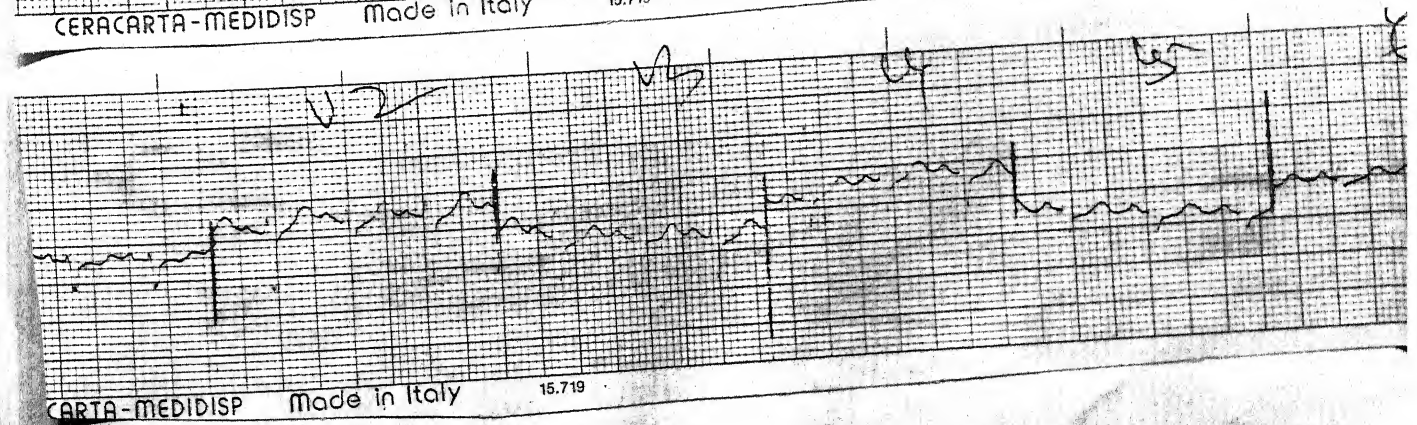
CARTA-MEDIDISP   Made in Italy   15.719

Kalpana

13. Name   : Chamelli

    P. rate   : 60/min, regular sinus rhythm

    P wave   : Normal morphology and duration

    Axis   : + 90°

    QRS complex   : 0.08 sec, normal configuration

    ST segment   : No coving, no depression,
                       no elevation.

    T wave   : Normal morphology

    Comment   : Within normal limit.

14. Name   : Vimla

    P. rate   : 100/min, regular sinus rhythm

    P wave   : Normal morphology & duration

    Axis   : + 45°

    QRS complex   : 0.08 sec, normal morphology
                       and duration.

    ST segment   : No elevation, no depression

    T wave   : Normal morphology

    Comment   : Normal E.C.G.
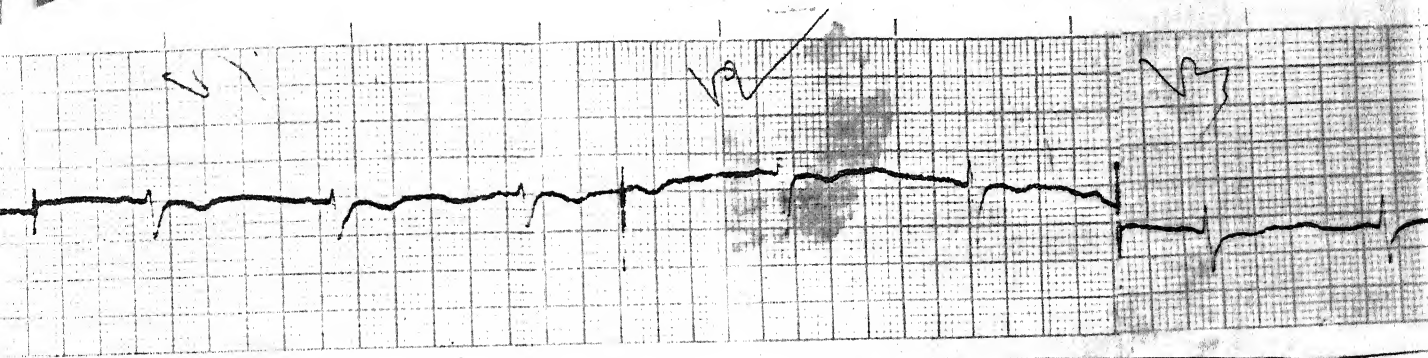
Chamelli
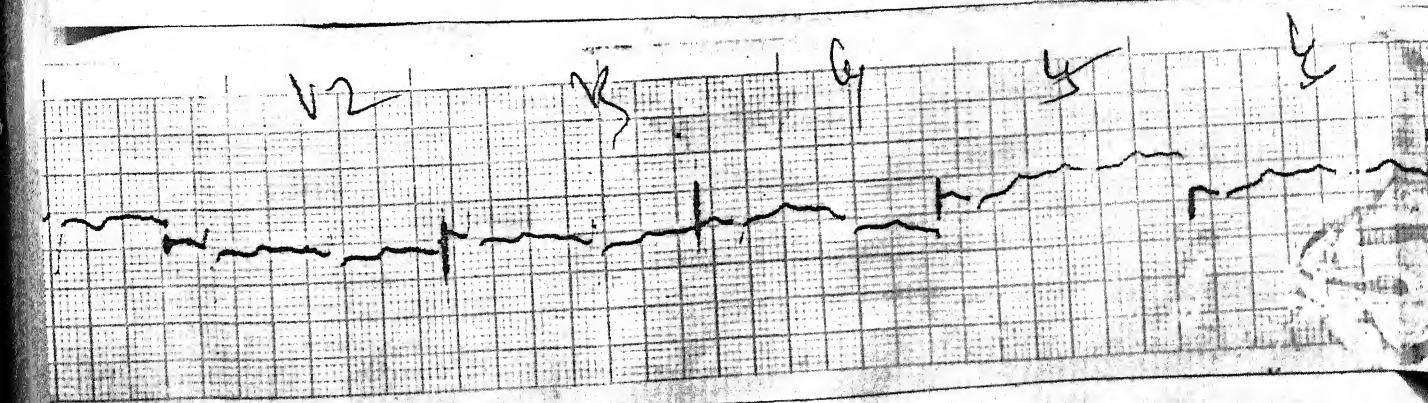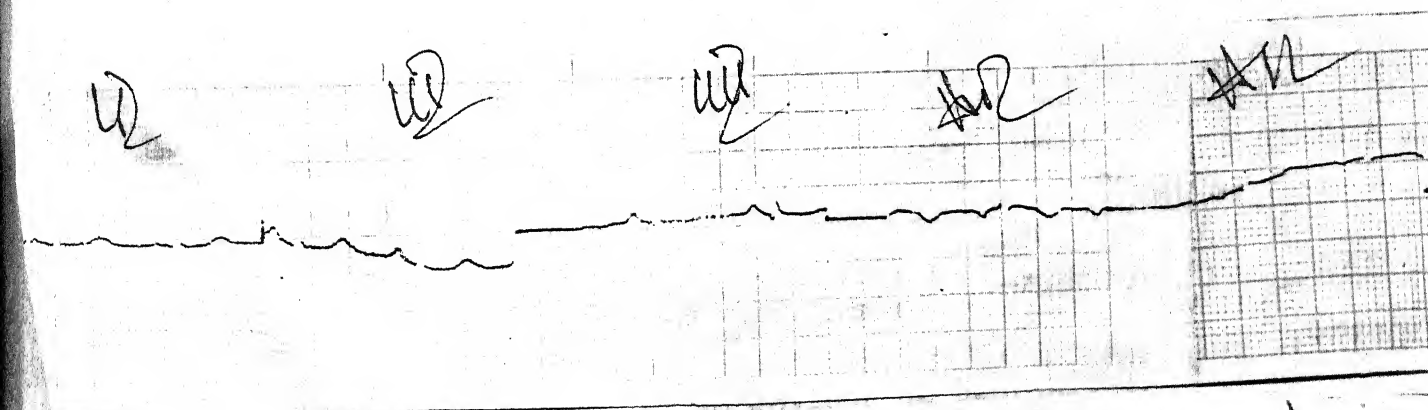
Vimla

Group B

After taking HRT for 3 months :

1. Name   :   Kusum

    P. rate   :   60/min, regular sinus rhythm

    P wave   :   Normal morphology and duration

    Axis   :   + 45°

    QRS complex   :   0.08 sec, normal morphology
                       and duration.

    ST segment   :   No coving, no depression and
                       no elevation.

    T wave   :   Tall T wave in V_2, V_3, V_4

    Comment   :   Within normal limit

2. Name   :   Teja

    P. rate   :   125/min, regular sinus rhythm

    P wave   :   Normal morphology and duration

    Axis   :   + 45°

    QRS complex   :   0.08 sec, normal configuration

    ST sgement   :   No coving, no depression,
                       no elevation.

    T wave   :   Normal morphology

    Comment   :   Sinus tachycardia
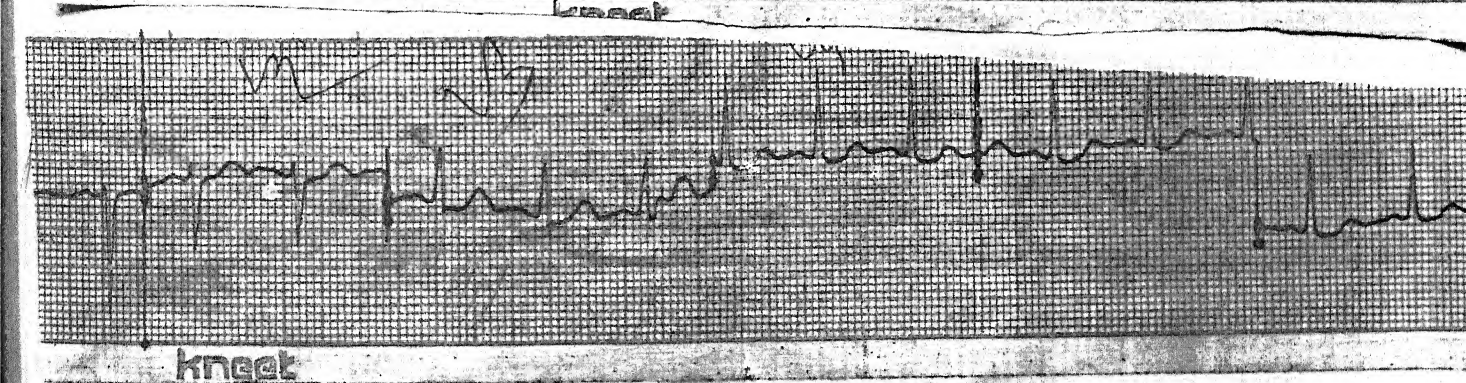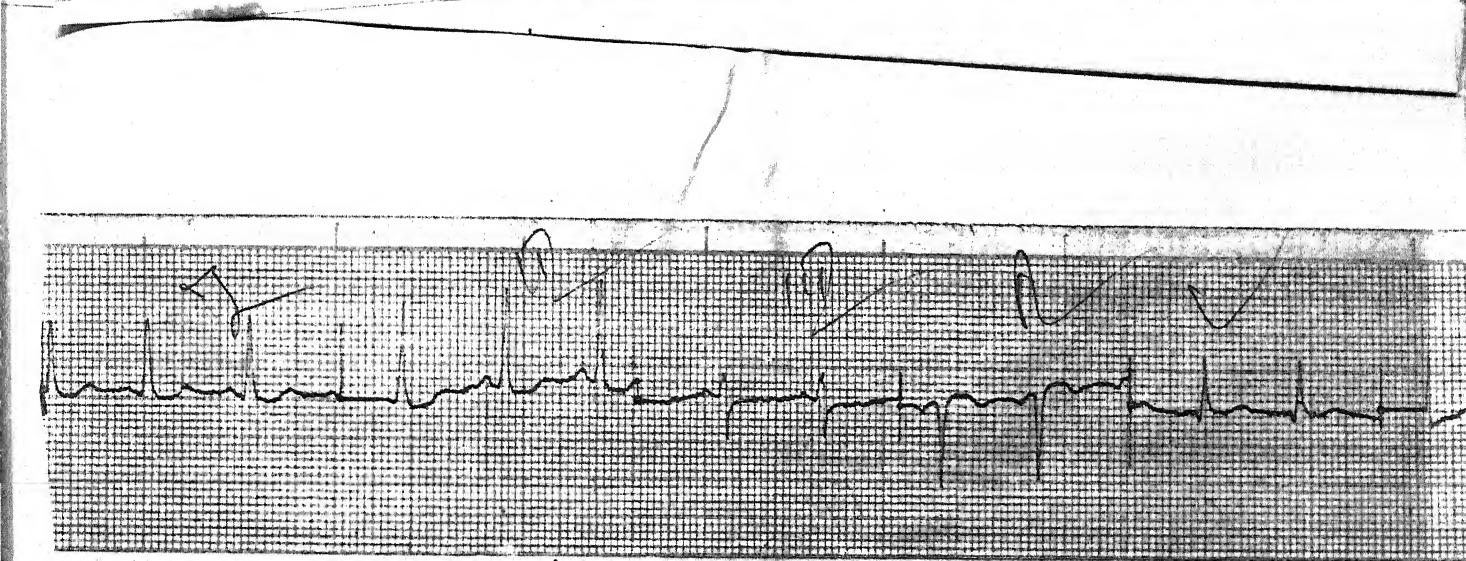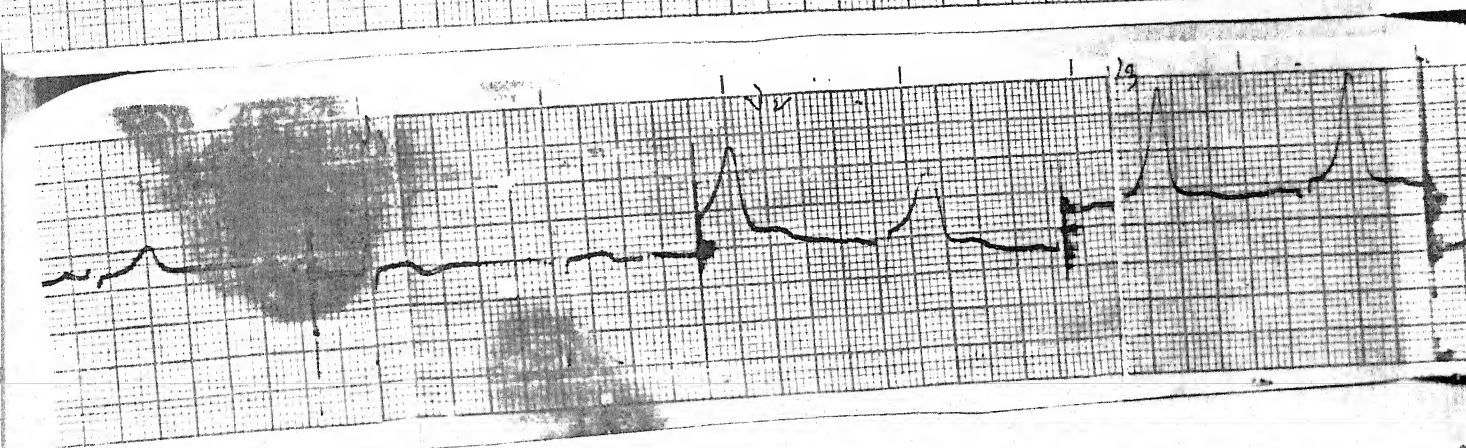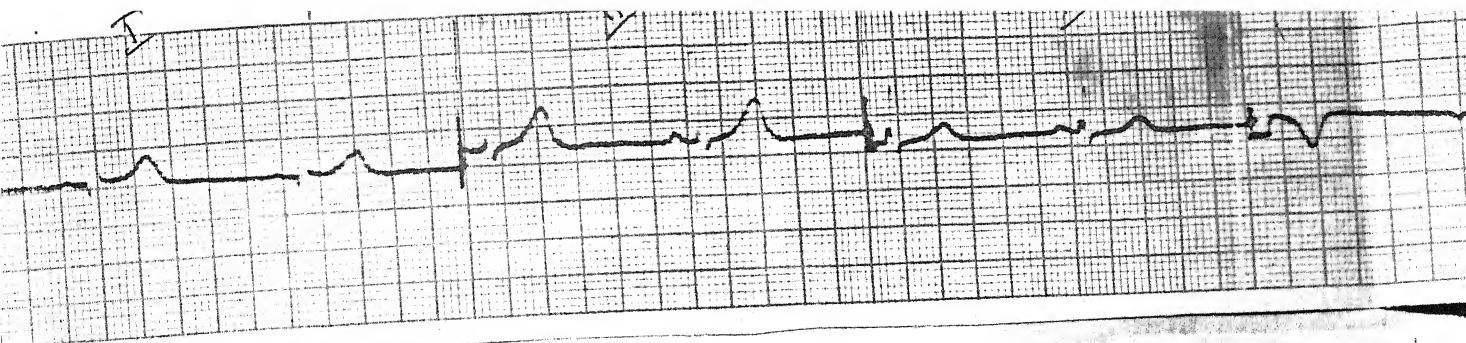
Teja

3.   Name   : Susheela

      P. rate   : 64/min, regular sinus rhythm

      P wave   : normal morphology & duration

      Axis   : + 30°

      QRS complex   : 0.08 sec, normal morphology
                        and duration.

      ST segment   : No elevation, no depression.

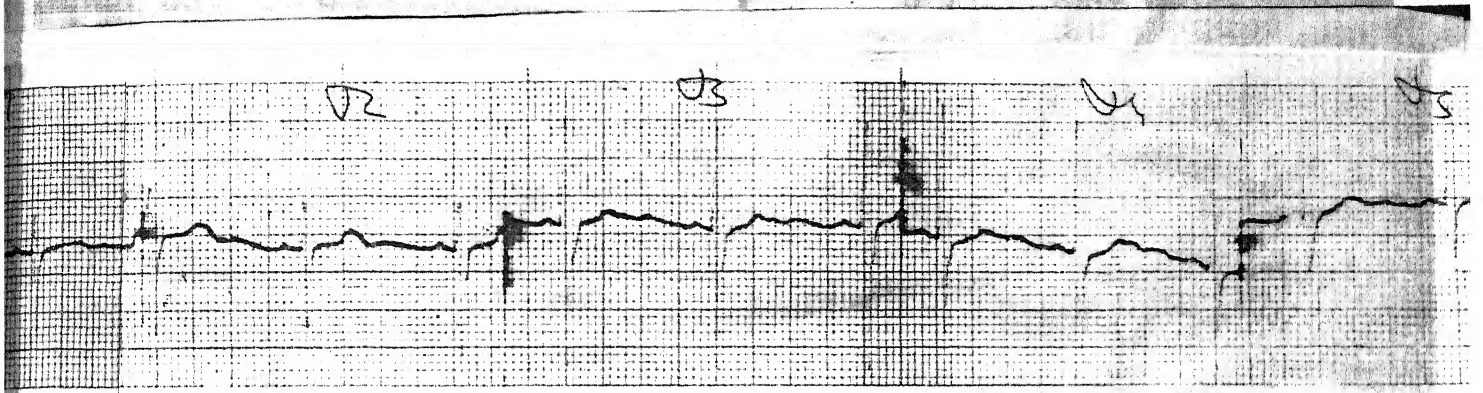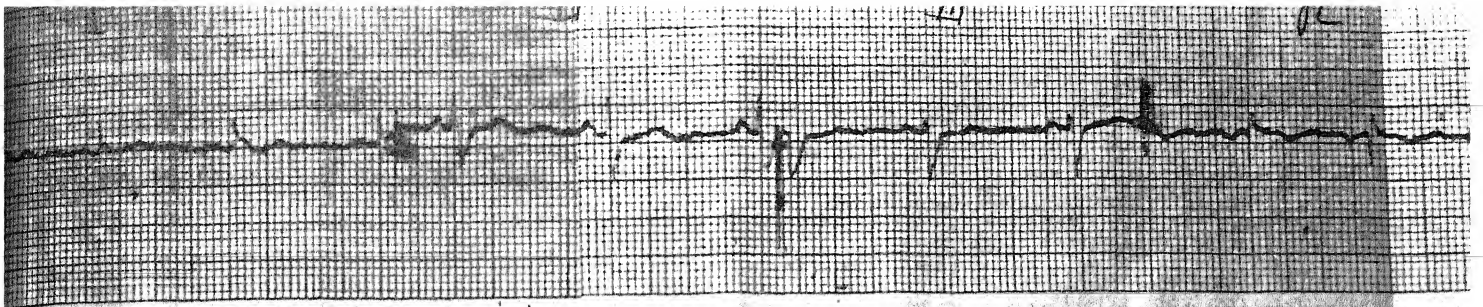   T wave   : Normal morphology

      Comment   : Normal E.C.G.

4.   Name   : Ajesha

      P. rate   : 75/min, regular sinus rhythm

      P wave   : Normal morphology and duration

      Axis   : + 45°

      QRS complex   : 0.08 sec, normal morphology
                        and duration.

      ST segment   : No elevation, no depression

      T wave   : Normal morphology

      Comment   : Within normal limit
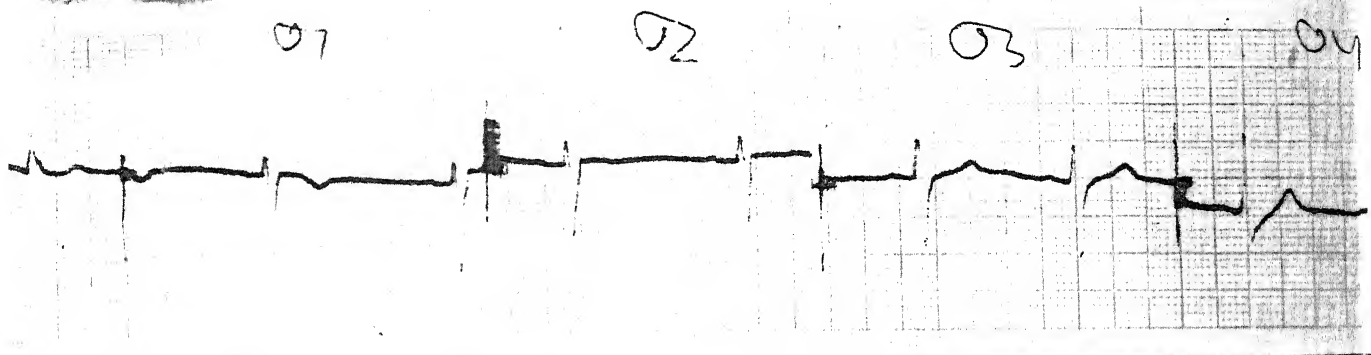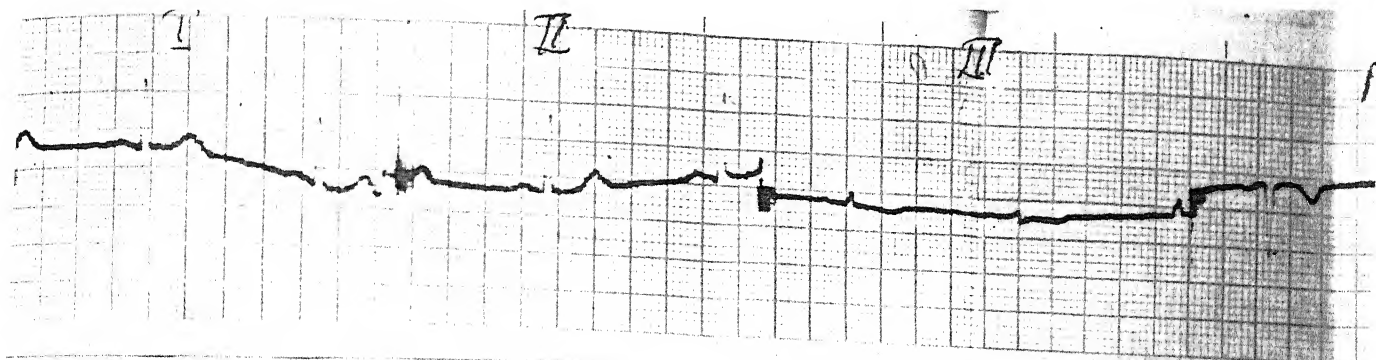
Susheela
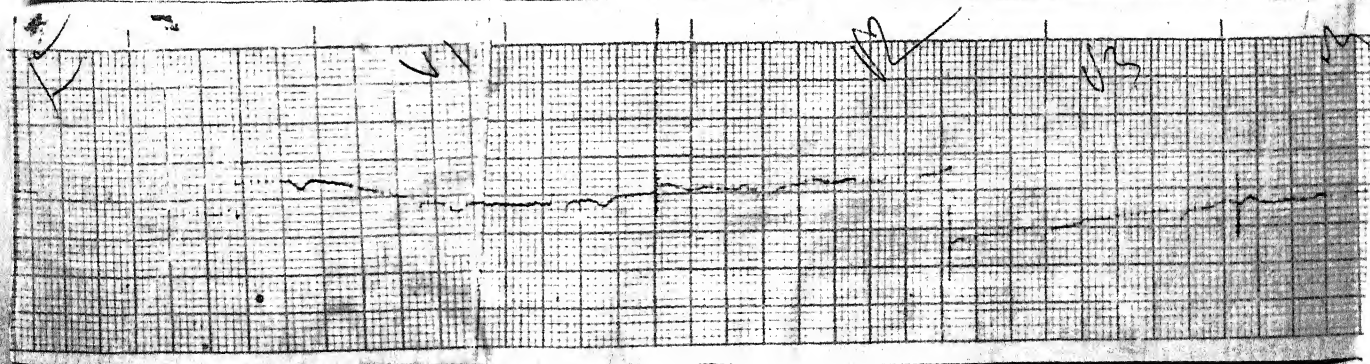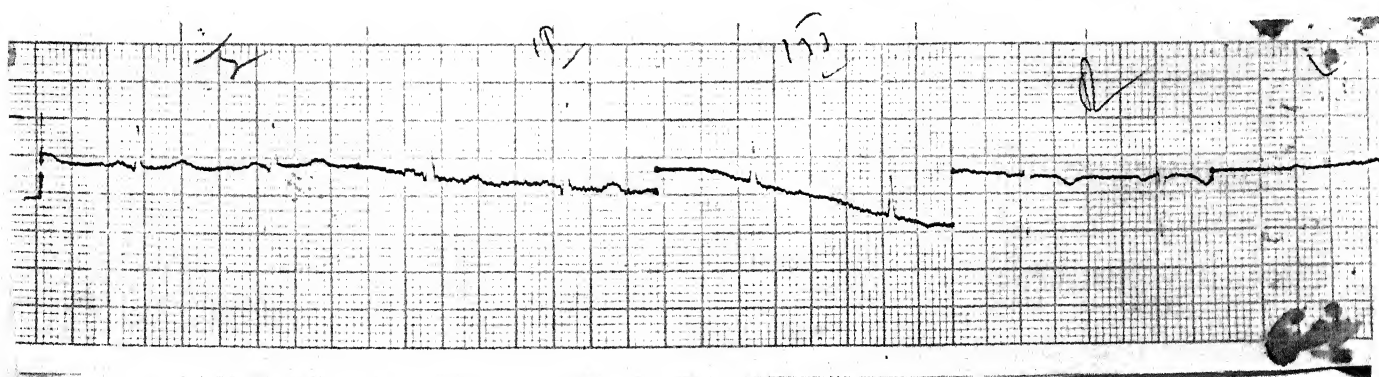
Ajesha
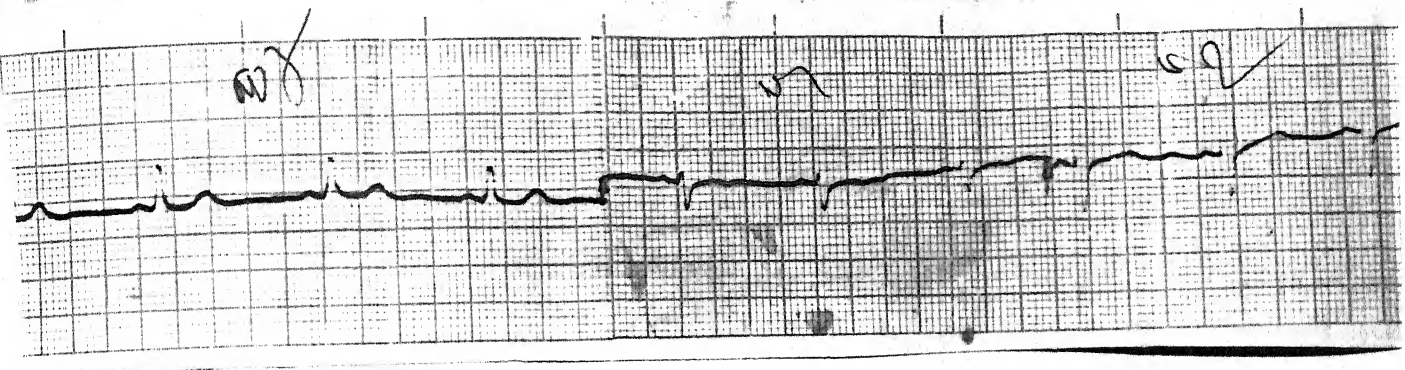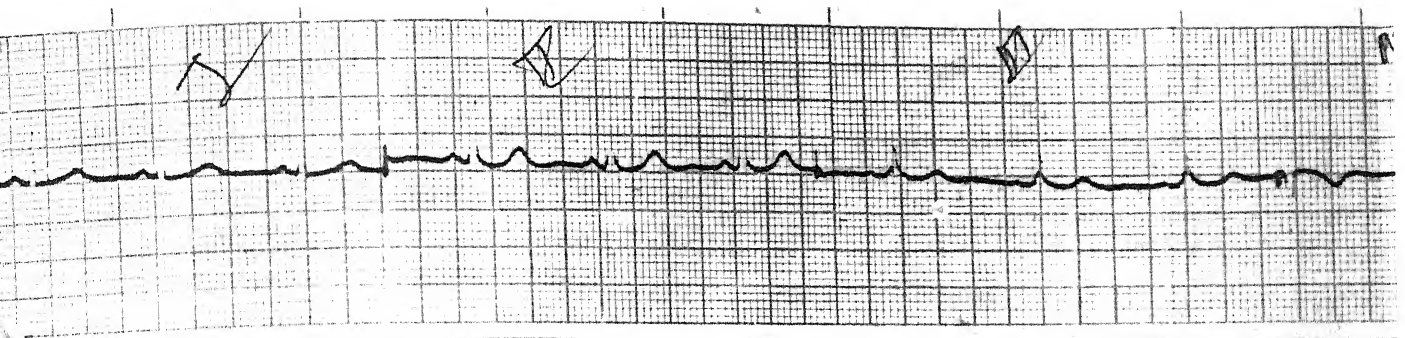
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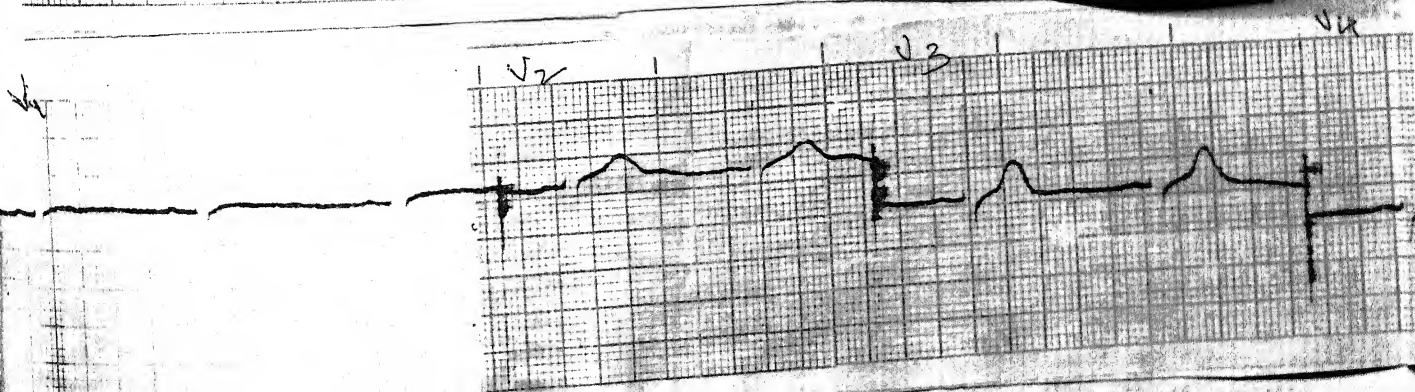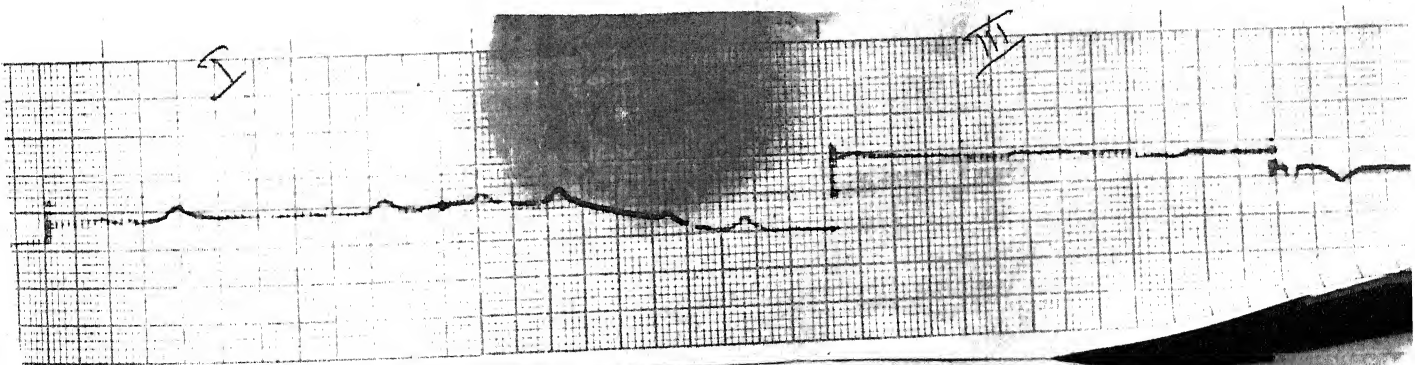
kailash

7. Name   : Manju

    P. rate   : 84/min, regular sinus rhythm

    P wave   : Normal morphology and duration

    Axis   : + 60°

    QRS complex   : Normal morphology & duration

    ST segment   : No elevation or depression

    T wave   : Normal morphology

    Comment   : Normal E.C.G.

8. Name   : Vimla

    P. rate   : 88/min, regular sinus rhythm

    P wave   : Normal duration & morphology

    Axis   : + 110°

    QRS complex   : 0.08 sec, normal morphology
                    and duration.

    ST segment   : No elevation or depression.

    T wave   : Normal morphology

    Comment   : Normal E.C.G.
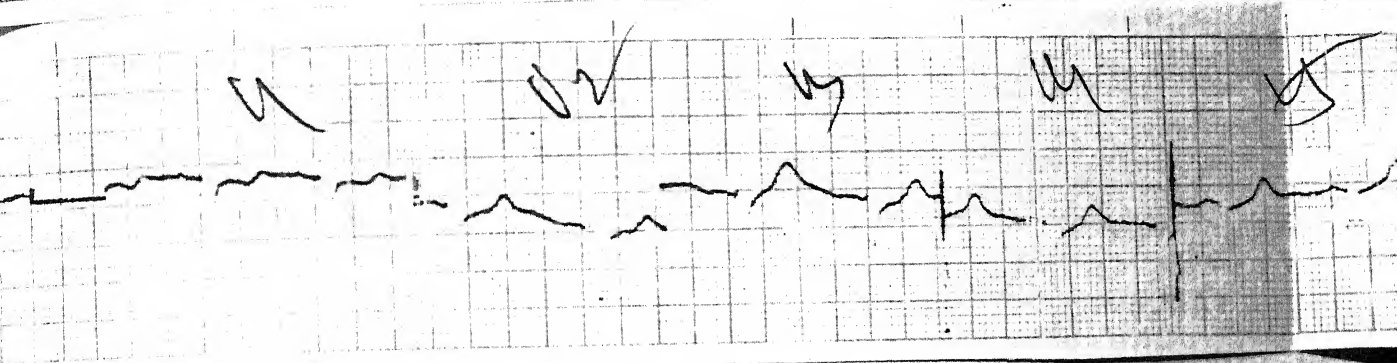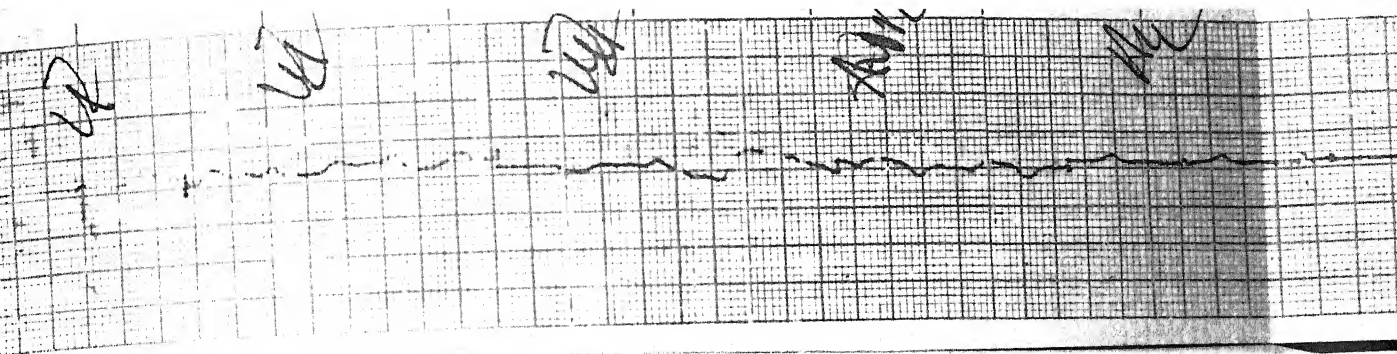
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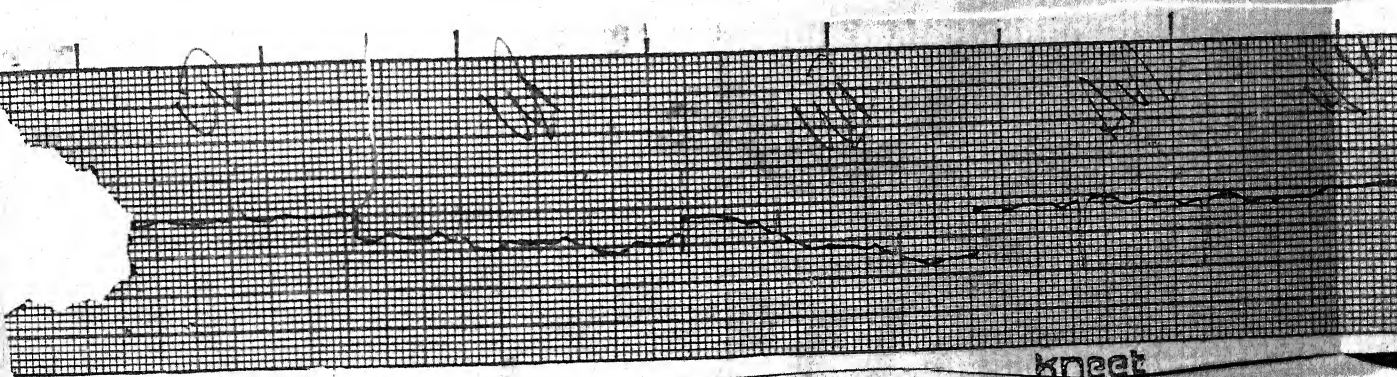
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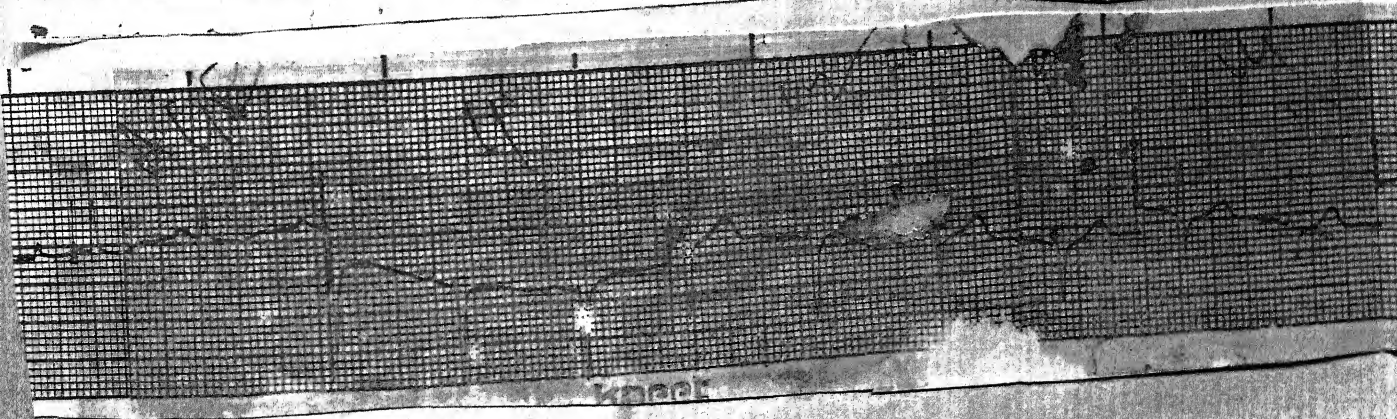
Vimla

DISCUSSION

D I S C U S S I O N

Hormone replacement therapy reduces many of distressing post menopausal symptoms and increases the quality of life style of post menopausal women and causes changes in lipid profile.

The lipid profile changes can be used as a tool in predicting cardiovascular risk. However, long term studies are required to come to definite confirmation. Basal lipid levels in normal females are as follows (Harrison).

Serum total cholesterol (STC)

    Basal : 200 mg/dl

    Border line : $>$ 200 - 239 mg/dl

    High : $>$ 240 mg/dl

Serum Triglycerides (STG)

    Basal : 40-172 mg/dl

Low density lipoprotein (LDL)

    Basal : $<$ 130 mg/dl

    Border line : 130-159 mg/dl

    High levels : $>$ 160 mg/dl

High density lipoproteins (HDL) : 30-80 mg/dl

In the present work "The effect of hormone replacement therapy (HRT) on lipid profile of menopausal females who have achieved menopause naturally or

surgically" was studied. STC, STG and HDL levels were estimated by chemical kits while LDL, VLDL and LDL/HDL ratio were calculated by standard formulae with the help of values of STC, STG and HDL cholesterol.

In addition to lipid profile in predicting cardiovascular risk, other parameters for cardiovascular problem like blood pressure and E.C.G. were taken before starting HRT and after withdrawal of HRT.

BLOOD PRESSURE

All the patients in group A and B had blood pressure in normal range. Mean blood pressure of at least readings in supine and resting period were taken in every visit. Blood pressure being dependent upon psychological, environmental, physical activities. There was a need for constant monitoring of the patients. The constant monitoring was not possible in this present study as the work was done in out patient department.

A further study involving larger number of patients and for longer period is needed to come to conclusion that HRT definitely causes changes in blood pressure of post menopausal females.

SERUM LIPID LIPOPROTEIN PROFILE

Serum Total Cholesterol

Group A

This group consisted of 25 patients who had

menopause naturally. Their age ranged from 45-55 years.
Mean duration of menopause ranged from 6 to 18 months.
It was found that in majority of subjects, the level of
STC was near to the upper limit of normal range. The
STC levels reduced after HRT for 3 months. The STC again
raised after withdrawal of HRT. Our results are
comparable with the results obtained by Boyd (1973),
Larson (1976), Rauramo (1976) and Hirvonen (1976).

Group B

In this group, out of 25 patients, 7 had basal
value of STC near to upper limit of normal range (200
mg/dl) whereas in group A majority (19) of the patients
had their STC levels near to 200 mg/dl. The reason of
this difference is that the group A patients had
sufficient time for hormonal stabilization. Samples
from patients of group A were withdrawn after an adequate
duration for circulating hormone to waive off. The mean
duration of menopause was 9 months. Whereas in group B
the samples were collected just after artificial menopause.
So the duration of menopause was lesser and mean duration
was 2 months. The circulating hormone had lesser time
to waive off. The value of STC showed reduction after
HRT as in group A. HRT reduced hot flushes, palpitation,
backache, insomnia. They gave a sense of well being.
Urinary problems - increased frequency of micturition,

urinary tract infection, and incontinence were decreased with HRT. There was an improvement in several activities in menopausal women with HRT. Our findings were similar with Rauramo and Punnonen (1976), Marck and Sha (1972), Fedan-Freyberg (1977), Smith (1977), Sarreb (1982) and Hammarback et al (1985).

The values of STC raised after withdrawal of hormonal replacement therapy.

Serum Triglycerides (STG)

The patients of this group A had higher basal values of STG than the patients of group B with similar height and weight. The reason behind this is that there were still circulating hormones in group B as their duration of menopause was lesser. In both the groups, the level of STG showed reduction with HRT and again it raised after withdrawal of HRT for 3 months. Our findings are similar with studies done by Welletin Larson Cohn (1977).

Serum LDL and VLDL Cholesterol

The majority of the patients of group A had basal LDL levels near to 130 mg/dl whereas in group B, only 7 patients had LDL basal levels near to 130 mg/dl. This clearly indicated that a certain duration (1-1/2 years)

is required for the circulating hormone to disappear
in menopausal women.

The levels of LDL and VLDL showed reduction
with HRT and raised after withdrawal of HRT for 3 months.

High Density Lipoproteins (HDL)

In both the groups the level of HDL
increased after HRT and decreased after withdrawal
of hormonal replacement therapy for 3 months.

E.C.G.

In group A : Electrocardiogram was taken in
10 patients before starting HRT. All the E.C.G.
recordings were within normal limit. E.C.G. was
recorded in four patients after hormonal replacement
therapy for 3 months and were normal limit.

In group B : All the patients were undergone
electrocardiogram before starting HRT as a pre-operative
assessment. All of them were normal. Eight patients
were subjected for E.C.G. after taking HRT for 3 months.
All of them were normal.

VAGINAL CYTOLOGY

In women who had acheived naturally menopause
the percentage of white discharge per vaginum decreased

from 20 to 8 percent with HRT. Their vaginal smear
showed dominance of basal cells indicating low
oestrogenic influence.

After withdrawal of HRT, the percentage
of patients with vaginal discharge due to vaginitis
increased from 8 to 20 percent. This shows
oestrogenic effect of HRT on vaginal mucosa.

In surgically induced menopausal women, 80%
of patients (20) had white discharge per vaginum. But
only 2 patients showed low oestrogenic influence in
their vaginal smear. The discrepancy between vaginal
smear and symptoms might be because of some amount of
white discharge from vaginal vault seen normally in
post hysterectomy patients.

After taking HRT for 3 months, 3 patients
complained of white discharge per vaginum. They showed
dominance of basal cells in their vaginal smear.

However, the percentage of patients with
low oestrogenic influence raised to 20% after withdrawal
of HRT for 3 months.

POST MENOPAUSAL SYMPTOMS

The psychogenic symptoms were commonly seen
in surgically induced menopausal women while symptoms
due to low oestrogenic influence are more commonly
encountered in women who has achieved menopause naturally

(Group A). This difference might be explained by the fact that surgically induced menopause had shorter duration of menopause and they had still circulating level of hormones though lesser in amount . So the symptoms associated with low oestrogens viz. backache, vaginitis and prolapse of genital organs are seen in surgically induced menopausal women in lesser percentage.

SUMMARY AND CONCLUSION

The present work was done to study the effect of
hormonal replacement therapy (HRT) (Premarin - 0.625 mg)
in women with surgically induced and natural menopause on
their symptoms and after effects of menopause. Special
reference was given to change of serum lipoprotein profile
and cardiovascular system.

Group A consisted of 25 subjects of postmenopausal
women who had come to out-patient department with post
menopausal symptoms. Group B consisted of 25 patients in
whom menopause has occurred surgically. They were operated
for benign conditions of uterus viz. fibroid functional
uterine bleeding and suspicious cervix.

Investigations were carried out three monthly .
They were before commencement of HRT, after giving HRT
for 3 months and after withdrawal of HRT for three months
in both the groups. Investigations comprised of blood
sample for lipoprotein profile, electrocardiogram and
vaginal cytology. Tablet Premarin (0.625mg) was given to
them once daily for 3 months.

In group A : patients had their basal total
serum cholesterol in the range from 172 to 228 mg/dl with
mean value of 191.12 mg/dl. Seven patients had STC levels
in borderline range (⟩200 mg/dl). Four patients had STC
levels near to 170 mg/dl. 14 patients had their STC

levels near to 200 mg/dl. After HRT all the 25 patients showed reduction in their STC levels. Reduction was in the range of 5-12 mg/dl with mean of 9.6 mg/dl. Two patients had same value of STC during HRT and after its withdrawal Before HRT 9 patients had their basal STG levels in the range of 100-110 mg/dl. Six patients had in the range of 90-100 mg/dl, 5 patients had in range of 80-90 mg/dl, Four patients had in range of 70-80 mg/dl and 1 patient had in the range of 60-70 mg/dl. After HRT 1 patient had same level of STG as before HRT. Remaining 24 patients showed reduction in their serum triglyceride levels in the range of 1-15 mg/dl with mean value of 5 mg/dl. After HRT three patients had same level of STG as during HRT. Remaining 22 patients showed an increase in STG levels. The minimum rise in STG value was 1 mg/dl and the maximum being 10 mg/dl with mean value of 5.18 mg/dl.

One patient had high level of basal LDL (165 mg/dl). 17 patients had LDL in range of 130-150 mg/dl with mean value of 138.03 mg/dl. All patients showed reduction in LDL levels. The minimum decrease was 1 mg/dl and maximum was 13.2 mg/dl. Basal level of VLDL ranged from 13.6 to 22 mg/dl with mean value of 18.41 mg/dl. Reduction in VLDL was seen in all patients. The minimum value of reduction was 1 mg/dl and maximum was   mg/dl with mean value of 3.5 mg/dl.

Basal value HDL ranged from 34 to 46 mg/dl with mean value of 39.6 mg/dl. Increase in HDL was seen in 22 patients after HRT. Rise ranged from 1 to 9 mg/dl with

rise of 4.5 mg/dl. One patient showed same level of HDL after HRT. 2 patients had decreased level of HDL with HRT. After HRT 2 patients showed same level of HDL as with HRT. 23 patients showed reduction in the HDL values. The minimum value of reduction was 1 mg/dl and maximum was 6 mg/dl with mean value of 3.5 mg/dl.

In group B : The basal values of STC ranged from 160 to 198 mg/dl with mean value of 171.36 mg/dl. After HRT one patient showed same value of STG and one patient showed reduction of 3 mg/dl in her STG value. Remaining 23 patients showed reduction in STG level . Reducing was in the range of 1 to 18 mg/dl with mean value of 5.65 mg/dl. After HRT the value of STC rose to a range of 2-19 mg/dl with mean value of 3.5 mg/dl. One patient had same value of STC even after HRT. After HRT one patient had same level of STG. 23 patients showed reduction in STG level. The minimum value of reduction was 1 mg/dl and mean was 8 mg/dl. One patient showed an increase in STG value after HRT by 2 mg/dl . After HRT 3 patients had same levels of STG. 22 patients showed rise in range of 2-10 mg/dl with mean value of 5.04 mg/dl.

The basal value of LDL ranged from 101 to 137 mg/dl with mean value of 122.8 mg/dl. 23 patients showed reduction in their values of LDL after HRT. The minimum reduction in value of/LDL after HRT was 0.2 mg/dl and the maximum was 19.8 mg/dl with mean value of 5.79 mg/dl. Three patients showed rise in LDL level. The minimum rise was 1.2 mg/dl

and maximum rise was 7.6 mg/dl with mean rise of 3.6 mg/dl. The value of LDL rose after withdrawal of HRT in 23 patients. The values ranged from 1 to 16.6 mg/dl, mean being 8.76 mg/dl. Two patients showed reduction in the rate of LDL after HRT. The basal level of VLDL ranged from 13 mg/dl to 22.4 mg/dl. The mean value was 17.53 mg/dl. After HRT reduction in the level of VLDL was seen in all patients ranging from 0.4 to 3.2 mg/dl with mean value of 1.2 mg/dl. After withdrawal of HRT the value of VLDL increased in 23 patients. The minimum rise was 1 mg/dl and the maximum rise was 0.8 to 3.8 mg/dl, mean 1.12 mg/dl. In 2 patients the value of VLDL remained same. The basal level of HDL ranged from 31 mg/dl to 46 mg/dl with mean HDL of 37.4 mg/dl. With HRT the value of HDL rose in 24 patients. The level ranged from 1 to 6 mg/dl with mean of 3.5 mg/dl. The level of HDL remained same in 3 patients. Three patients had decreased level of HDL in range of 2 to 6 mg/dl with mean value of 4 mg/dl. After withdrawal of HRT 1 patient had same value as with HRT. In the remaining 24 patients HDL levels ranged from 1 to 8 mg/dl with mean value of 4.1 mg/dl.

Vaginal cytology was done in patients having complaint of white discharge per vaginum. Their smear showed decreased oestrogenization. The frequency of decreased oestrogenization was more in group A. This shows that as the duration of menopause is longer in group A (mean - 9 months).

The subjects of group A had their circulating hormone wane off. After HRT the vaginal cytology showed increased oestrogenization and the number of patients with white discharge per vaginum decreased in both the groups.

From the present study, it was observed that HRT causes reduction in levels of STC, STG, LDL and VLDL and rise of HDL. The HRT also causes much reduction in post menopausal symptoms and reduces urinary symptoms.

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MASTER CHART

MASTER - CHART

GROUP A : General Characteristics and routine Investigations.

Sl. No.	Name	Age (yrs.)	Duration of meno-pause (months)	Socio-economic status	Height (Inches)	Weight (kg)	Dietary habit	Hb (gms)	Urine Albu-min	Urine Sugar
1.	Hazra	48	16	Middle	61	52	Vegeta-rian	11	Nil	Nil
2.	Chya Rani	47	18	Poor	60	51	"	10	"	"
3.	Dropadi	45	9	Poor	59	49	"	9	"	"
4.	Kastoori	49	12	Poor	58	48	"	10	"	"
5.	Kasani Bai	50	14	"	64	54	"	9	"	"
6.	Sheela	49	9	"	64	55	"	11	"	"
7.	Gori Bai	48	18	"	62	52	"	10	"	"
8.	Zebun	47	11	"	63	54	"	9	"	"
9.	Seema	48	9	"	63	54	"	11	"	"
10.	Noor Jehan	51	10	"	63	48	"	10	"	"
11.	Bhawani Bai	50	9	"	62	49	"	9	"	"
12.	Leeni	48	12	"	61	50	"	11	"	"
13.	Junni	49	9	"	64	55	"	10	"	"
14.	Sunni	50	10	"	59	50	"	11	"	"
15.	Manju	48	9	"	60	48	"	10	"	"
16.	Janak Kishori	54	6	"	59	49	"	9	"	"
17.	Pushpa	48	14	"	62	52	"	11	"	"
18.	Prewati	49	9	"	58	49	"	11	"	"
19.	Ramshree	55	12	"	62	52	"	9	"	"
20.	Nisha	47	9	"	63	54	"	9	"	"
21.	Flower	48	10	"	61	54	"	10	"	"
22.	Kalpana	49	9	"	62	55	"	10	"	"
23.	Laxmi	48	9	"	63	50	"	10	"	"
24.	Vimla	49	9	"	59	50	"	11	"	"
25.	Bhagwati	47	9	"	64	55	"	9	"	"

Group A : Serum lipid lipoproteins profile

Sl. No.	STC 0-3	STC 4-6	STC 7-9	STG 0-3	STG 4-6	STG 7-9	LDL 0-3	LDL 4-6	LDL 7-9
1.	228	220	220	105	98	100	165.0	160.4	162.0
2.	195	190	190	71	70	70	135.8	133.0	134.0
3.	188	180	186	79.5	74	82	138.4	125.2	135.6
4.	200	196	205	68	66	69	151.4	144.8	157.2
5.	179	175	185	72	70	80	123.6	119.0	129.0
6.	202	198	205	100	94	100	140.0	137.2	145.0
7.	198	188	199	105	95	100	139.0	129.0	142.0
8.	172	168	180	87	84	90	108.6	104.2	120.0
9.	200	190	205	110	95	100	135.0	127.0	143.0
10.	181	180	190	100	95	98	122.0	121.0	132.6
11.	185	180	190	78	82	82	133.4	125.0	135.6
12.	172	170	180	86	84	86	110.8	107.0	122.8
13.	176	170	180	98	90	96	115.4	109.0	130.8
14.	168	162	172	90	90	100	110.0	99.0	150.0
15.	200	185	195	102	95	100	143.6	121.0	160.0
16.	191	190	200	102	100	108	127.6	125.0	145.6
17.	204	200	210	105	102	102	143.0	137.6	147.8
18.	186	182	200	95	90	95	131.0	126.0	155.0
19.	190	185	195	90	85	86	132.0	126.0	143.8
20.	200	195	200	88	86	90	146.4	129.8	157.0
21.	191	187	200	95	88	92	132.0	127.4	149.6
22.	187	182	192	88	83	86	135.4	130.4	153.8
23.	187	185	195	88	86	90	135.4	131.8	162.0
24.	196	190	200	106	100	108	134.8	128.0	156.6
25.	202	198	204	98	92	96	140.4	135.6	144.8

sl. No.	VLDL			HDL			LDL/HDL		
	0-3	4-6	7-9	0-3	4-6	7-9	0-3	4-6	7-9
1.	21.0	19.6	20.0	42	40	38	3.92	4.01	4.26
2.	14.2	14.0	14.0	45	43	42	3.01	3.09	3.19
3.	15.9	14.8	16.4	36	40	34	3.84	3.13	3.97
4.	13.6	13.2	13.8	35	36	34	4.32	3.81	4.61
5.	14.4	14.0	16.0	41	42	40	3.01	2.83	3.22
6.	20.0	18.8	20.0	42	42	40	3.33	3.26	3.62
7.	21.0	19.0	20.0	38	40	37	3.65	3.22	3.62
8.	17.4	16.8	18.0	46	47	42	2.36	2.21	2.85
9.	22.0	19.0	20.0	43	44	42	3.13	2.88	3.40
10.	20.0	19.0	19.4	39	40	38	3.12	3.02	3.47
11.	15.6	16.4	16.4	36	38	38	3.70	3.28	3.55
12.	17.2	16.8	17.2	44	46	40	2.51	2.32	3.05
13.	19.6	18.0	19.2	41	43	40	2.81	2.53	3.25
14.	18.0	18.0	20.0	40	45	40	2.75	2.20	3.75
15.	20.4	19.0	20.0	36	45	40	3.98	2.68	4.00
16.	20.4	20.0	21.4	43	45	43	2.96	2.77	3.37
17.	21.0	20.4	20.4	40	42	42	3.57	3.27	3.50
18.	19.0	18.0	19.0	36.	38	36	3.63	3.31	4.30
19.	18.0	17.0	16.2	40	42	40	3.30	3.00	3.75
20.	17.6	17.2	18.0	36	38	35	4.06	3.41	4.48
21.	19.0	17.6	18.4	40	42	40	3.30	3.03	3.74
22.	17.6	16.6	17.2	34	35	34	3.98	3.72	4.52
23.	17.6	17.2	18.0	34	36	30	3.98	3.65	5.40
24.	21.2	20.0	21.4	40	42	40	3.37	3.04	3.91
25.	19.6	18.0	19.2	42	44	40	3.34	3.08	3.62

Group B : General characteristics and routine investigations.

Sl. No.	Name	Age (yrs.)	Duration of meno- pause (months)	Socio- economic status	Height (Inches)	Weight (kg)	Dietary habit	Hb. (gm%)	Urine Albu- min	Urine Sugar
1.	Jamna	46	1	Poor	62	53	Veget- arian	9	Nil	Nil
2.	Laxmi	45	1	"	63	54	"	10	"	"
3.	Rankali	46	1	""	61	50	"	9	"	"
4.	Ram Bal	46	1	Middle	59	48	"	10	"	"
5.	Manju	45	1	Poor	64	49	"	11	"	"
6.	Champa Bai	45	1	"	63	54	"	10	"	"
7.	Shiv Kumari	46	1	"	62	52	"	9	"	"
8.	Ganeshi	45	1	"	64	53	"	10	"	"
9.	Prema Devi	46	1	"	62	54	"	11	"	"
10.	Ram Kumari	46	1	"	59	49	"	11	"	"
11.	Ram Shree	45	1	"	64	54	"	11	"	"
12.	Susheela	46	1	Middle	59	50	"	9	"	"
13.	Ram Kumari	45	1	Poor	62	52	"	11	"	"
14.	Ram Pyari	46	1	"	63	51	"	10	"	"
15.	Kusum	48	1	"	64	55	"	11	"	"
16.	Kailashi	48	1	"	59	48	"	10	"	"
17.	Kalpana	46	1	"	60	50	"	11	"	"
18.	Ayesha	50	1	"	59	50	"	10	"	"
19.	Bhagwati	46	1	"	62	52	"	9	"	"
20.	Vimla	46	1	"	63	54	"	10	"	"
21.	Kalashmi	42	1	Middle	62	52	"	10	"	"
22.	Katia	48	1	Poor	60	51	"	9	"	"
23.	Raja Beti	48	1	"	64	55	"	11	"	"
24.	Teja	46	1	"	59	50	"	10	"	"
25.	Premwati	46	1	"	63	54	"	11	"	"

Group B : Serum lipid lipoproteins profile.

Sl. No.	STC			STG			LDL		
	0-3	4-6	7-9	0-3	4-6	7-9	0-3	4-6	7-9
1.	142	175	168	84	80	80	119.2	119.0	114.0
2.	192	186	188	88	90	94	137.4	125.0	129.6
3.	188	182	184	96	91	95	124.8	123.8	127.0
4.	180	178	175	90	88	92	128.0	125.4	123.6
5.	170	165	176	100	98	105	119.0	110.4	124.6
6.	191	190	188	84	80	86	137.2	131.0	135.8
7.	176	172	182	100	94	100	124.0	123.2	132.0
8.	175	175	180	88	88	90	115.4	105.4	122.0
9.	194	180	186	91	85	94	135.8	129.0	133.2
10.	160	158	164	69	60	65	113.8	111.0	121.0
11.	152	145	154	65	55	60	101.0	94.0	107.0
12.	160	170	170	88	80	90	111.4	119.0	120.0
13.	162	160	170	86	82	90	106.8	108.6	122.0
14.	180	178	186	91	90	95	126.8	120.0	132.0
15.	178	160	170	80	78	80	124.0	104.2	116.0
16.	182	180	190	87	79	85	124.6	120.2	133.0
17.	170	160	165	77	72	76	120.6	107.6	117.8
18.	198	192	194	112	105	110	129.6	128.0	132.0
19.	164	165	170	76	75	80	116.0	118.0	121.0
20.	194	195	198	104	100	100	131.2	133.0	139.0
21.	196	190	185	91	88	92	137.8	129.4	127.5
22.	188	178	190	87	84	90	132.6	121.2	140.0
23.	194	187	195	90	85	90	132.0	125.0	137.0
24.	174	170	180	84	80	86	117.2	111.0	122.8
25.	160	152	160	84	80	90	103.2	98.0	106.0

Sl. No.	VLDL			HDL			LDL/HDL		
	0-3	4-6	7-9	0-3	4-6	7-9	0-3	4-6	7-9
1.	16.8	16.0	16.0	36	40	38	3.31	2.97	3.00
2.	17.6	18.0	18.4	37	43	40	3.71	2.90	3.24
3.	19.2	18.2	19.0	40	40	38	3.12	3.09	3.34
4.	18.0	17.6	18.4	34	35	33	3.76	3.58	3.74
5.	20.0	19.6	21.0	31	35	32	3.83	3.15	3.89
6.	16.8	16.0	17.2	37	43	35	3.70	3.04	3.88
7.	20.0	18.8	20.0	32	30	30	3.87	4.10	4.40
8.	17.6	13.6	18.0	42	36	40	2.74	2.92	3.05
9.	18.2	15.0	18.8	40	36	34	3.39	3.58	3.92
10.	18.8	12.0	13.0	32	35	30	3.56	3.17	4.03
11.	13.0	11.0	12.0	38	40	35	2.65	2.68	3.06
12.	17.6	16.0	18.0	31	35	32	3.59	3.40	3.75
13.	17.2	16.4	18.0	38	35	30	2.81	3.10	4.06
14.	18.2	18.0	19.0	35	40	35	3.62	3.00	3.77
15.	16.0	15.6	16.0	38	40	38	3.26	2.60	3.05
16.	17.4	15.8	17.0	40	44	40	3.11	3.73	3.32
17.	15.4	14.4	15.2	34	38	32	3.55	2.83	3.68
18.	22.4	21.0	22.0	46	43	40	2.82	2.97	3.30
19.	15.2	15.0	16.0	32	32	33	3.65	3.69	3.66
20.	20.8	20.0	20.0	42	42	39	3.12	3.16	3.56
21.	18.2	17.6	18.4	40	43	39	3.44	3.01	3.27
22.	17.4	16.8	18.0	38	40	32	3.49	3.03	4.37
23.	18.0	17.0	18.0	44	45	40	3.00	2.78	3.42
24.	16.8	16.0	17.2	40	43	40	2.93	2.58	3.07
25.	16.8	16.0	18.0	40	38	36	2.58	2.58	2.75

WORKING PROFORMA

Name: Age :

Address :

Diagnosis :   Date of Operation:

Presenting Complaints :

Past history :

       Diabetes

       Hypertension

       T.B.

Family History of Cardiovascular disease :

H.R.T. :

General Examination :

       G.C.   Pallor

       Pulse   Icterus

       B.P.   Cyanosis

       Temperature   Gen Lymph node

       R.R.   Weight

Systemic Examination :

       C.V.S.

       C.N.S.

       Respiration

       G.I.T.

Per speculum Examination :

Observations (3 monthly) :

       STC   STG

       LDL   VLDL

       E.C.G. :

Vaginal Cytology (3 monthly) :